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Bright's Disease *

A Review of the Pathology and Clinical Findings.

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In proceeding to a discussion of the pathology of Bright's Disease the difficulty is at once encountered of making a proper classification. This is due to the fact that the various processes of inflammation and degeneration do not stand apart as entities but are nearly always associated to a greater or less degree. A further difficulty lies in the fact that a given pathological condition in the kidney apparently does not always produce the same clinical picture and, as a result, no classification will meet all the requirements of the clinic and at the same time accord with the anatomical findings. Proof of this is seen in the wide diversity of opinion expressed by different writers. The recent work of Volhard and Fahr has produced a classification quite at variance with that of Mallory, Osler, or Delafield and Prudden. The sequence of pathological changes is still a subject of debate, and certain conditions described by one writer are not recognized by others. It seems best, therefore, to describe the essential nature of the lesions found in the degenerative processes and by nephroses in acute and chronic inflammations or nephritis, and to mention such clinical findings as are commonly considered to be diagnostic of at least the major lesion in each case.

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The Nephroses.

Poisons or bacterial toxins present in the blood are excreted through the glomeruli, and, acting on the renal epithelium, give rise to changes that are degenerative rather than inflammatory. The parts involved are commonly the proximal convoluted tubules and the limbs of Henle. There may be changes in the distal convoluted tubules, and, more rarely, in the epithelium covering the glomeruli.

The following types are recognized:

1. Cloudy Swelling.—This form is most common in the acute infectious diseases such as diphtheria, scarlet fever, pneumonia and typhoid, in certain forms of septicemia or toxemia and in sublimate poisoning. In moderate degrees of the lesion the epithelium of the tubules is swollen and granular. If more severe, the cells may disintegrate and peel off into the lumen, or they may become necrotic and the nuclei fail to stain.

The gross appearance of the kidney varies with the extent of the lesion. It may be slightly or greatly enlarged. On section the cortex is usually thickened and pale with obliteration of the normal markings.

The condition of cloudy swelling does not persist. If the patient recovers from the causative condition, kidney recovery should be complete.

2. Fatty degeneration of tubules.—This is usually associated with chronic genereal diseases, such as pernicious anaemia, leukemia and diabetes. It is also seen in chronic glomerulo-nephritis where circulation is interfered with in the glomerulus and the tubule suffers in consequence. The degeneration may be diffuse or patchy: if diffuse, the cortex, in which it is generally most marked, is thickened, opaque and yellowish; if patchy there are opaque yellow streaks or spots in the cortex. Microscopically, fat droplets are seen in the cells of the convoluted tubules, or, if the condition be more advanced, the cells are filled with fat droplets and may peel off into the lumen or may disintegrate and discharge the fat into the lumen. The process may involve the capsule epithelium as well .

3. Amyloid deposit.—This is usually incidental to chronic disease of bacterial origin—tuberculosis, syphilis, or chronic osteo-myelitis. The capillaries of the tufts are most commonly affected. The presence of amyloid causes pressure atrophy and impedes function. It commonly results in fibrosis of the surrounding structures. In the early stages the kidneys are large and pale with the cortex thickened. Later the organ may be shrunken, due to fibrosis.

In these types of nephrosis the urine is diminished in amount, sometimes to the point of anuria. The specific gravity tends to be high except in bichloride poisoning where necrosis has occurred. Albuminuria appears when toxic injury occurs and is usually very marked. Cells appear in the urine, first separately, then as casts. Granular casts are a later development. Blood never appears. Oedema sometimes occurs, probably due to failure to excrete chlorides. The blood pressure is never raised.

The type of nephrosis cannot be diagnosed clinically with any degree of accuracy. When amyloid deposit has existed for some time large wax-like casts are often seen in the urine and are a diagnostic sign.

It should be noted here that Professor Klotz insists that nephrosis does not go to a chronic state as described by some authors. Where nephrosis is followed by a fibrosis he is convinced that, in every case, infection has been super-imposed upon the primary condition of nephrosis. A pure nephrosis, therefore, must always be able to regenerate completely. It might be supposed however, that where the condition responsible for the nephrosis is chronic and long cintinued, as in diabetes, or in chronic bone conditions, the degenerative condition in the kidney might itself become of such nature as to be considered chronic.

The Nephritides.

All nephritis is accompanied by nephrosis, but nephritis is more extensive than mere degeneration. The important inflammatory lesions are found in the cortex, relatively little reaction being seen in the medulla. All the structures of the secretory unit are involved, capillaries, capsule and tubules; and the interstitial tissue does not escape entirely. The reaction, however, may be more marked in one tissue than in the others.

1. Acute Nephritis

All nephritis is probaly due to bacterial action. The streptococcus of scarlet-fever is known to produce non-suppurative lesions in the kidney. Nephritis is commonly a sequelae of measles, small-pox or endocarditis. In the acute stage of nephritis two types are recognized, focal and diffuse.

a. **Acute Focal Nephritis.**—This condition most often occurs in association with endocarditis, as a result of bacterial emboli set free into the blood stream from the endocardium. Where the bacteria lodge in the kidney vessels, usually in the capillary loops of the glomeruli, they cause obstruction and set up a local inflammation. At first there is hyperemia or haemorrhage, fol-

lowed by necrosis. Leucocytes gather, the necrosed tissue disintegrates and an abscess forms. Few or many glomeruli may be involved. The individual glomerulus may be involved in part or altogether. The distribution of the lesions is patchy. Minute abscesses may coalesce so as to give rise to relatively large areas of involvement. Both kidneys are commonly affected but the condition may be unilateral due to an accident in distribution of the emboli or to a local susceptibility.

It should be noted that the glomerulus is never involved alone. Because of the nature of the blood supply of the secretary unit any obstruction in the glomerulus causes interference with the nutrition of the tubules and pathological changes result.

The clinical findings in a case of focal nephritis are fairly constant. There is no disturbance of secretion. The output of water, sodium chrolide and nitrogen is normal due to the great reserve of the kidney. Oedema does not occur. Convulsions are rare and when they do occur are the result of brain embolism. Blood is always present in the urine as are white blood cells and casts. Albumin is nearly always present.

The outcome of a case depends on the progress of the exciting condition. If the patient recovers from the lesion which caused the nephritis, his kidney will remain fairly efficient.

b. Acute Diffuse Nephritis. — This condition is also termed acute diffuse glomerulo-nephritis (Volhard & Fahr), but as previously noted it never involves the glomeruli alone. It may occur in the acute infectious diseases and is especially common in scarlet fever, and in acute upper respiratory tract infections.

The lesions vary greatly in extent and in the relative involvement of the different renal structures. The changes in the different structures may occur simultaneously and are always closely associated each with the other.

In the glomeruli the early changes include swelling of the cells covering the capillary loops. Nuclei enlarge and mitoses are sometimes seen. The capillaries are sometimes distended with leucocytes and swollen endothelial cells. Hyaline thrombi are often present. The swollen tufts of epithelium may undergo fatty degeneration and peel off into the glomerular space. At times proliferation and exfoliation of the epithelial elements is very marked and the cells collect in crescentic masses within the capsule crowding the tuft toward its hilus. Sometimes there is a considerable accumulation of albuminous exudate between the tuft and the capsule, mixed with degenerated epithelium and cell detritus. Fibrin, red blood cells and leucocytes may be present with other exudate within the capsule.

The lesions of the tubules in the early stages of acute nephritis are largely degenerative. The epithelium, especially of the convoluted tubules is swollen and coarsely granular, or may even show fatty degeneration. The degeneration may go on to necrosis and the cells disintegrate or peel off into the lumen. Thus, as a result of the inflammatory processes in glomeruli and tubules the lumina of the tubules may contain epithelial cells, red and white blood cells, debris, and all forms of casts.

The interstitial tissue may be oedematous or it may be infiltrated with leucocytes or exudate. Newly formed interstitial cells may be seen, small and spheroidal, or larger, with conspicuous excentric nuclei, near the glomeruli or near the interlobular veins. A general thickening of interstitial tissue occurs early in some forms of diffuse nephritis, especially in those following scarlet fever and diphtheria.

There are so many variations in the type of the lesions in acute diffuse nephritis that, according to the relative prominence of the different structural changes, certain sub-types have been recognized. When glomerular changes are prominent the condition has been termed glomerular (glomerulo-neph-

ritis); when the degenerative process in the tubular epithelium is extreme it has been called parenchymatous; and when there has been considerable haemorrhage, a hemorrhagic type is mentioned. With or without marked involvement of the parenchyma or interstitial tissue there may be an exudative inflammation in which serum, leucocytes, and red blood cells gather in the glomeruli or tubules and, with various forms of casts, pass off in the urine. This has been called the exudative type. Again the exudate may collect chiefly in the interstitial tissue, and little exudate or casts be found in the urine. Finally with any one or more of the above types of lesions there may appear marked changes in the interstitial tissue with such proliferation as to cause tubular atrophy. This has been called by some writers the productive type, by others the interstitial type. It is most frequent as a complication of scarlet fever but may follow diphtheria or puerperal infections, or may occur as an apparently independent process.

In gross appearance the kidney in acute diffuse nephritis may be nearly normal. More commonly it is enlarged slightly or considerably. The capsule is free and the cortex is thickened and red, or pale, or mottled. When there is oedema of the interstitial tissue the cortex may appear translucent. In haemorrhagic forms of cortex is mottled with red.

In many forms of this condition, particularly if interstitial involvement is not extensive, resolution may occur.

While as stated above, all nephritis is probably due to bacterial action, this has not been determined, and it may be that in some cases the process is due to toxic substances formed elsewhere in the body and affecting the kidney when it excretes or attempts to excrete them. Such substances may be the product of bacterial action or of abnormal body-cell metabolism, the latter perhaps being the exciting factor in the nephritis following extensive burns or exposure to cold.

Many bacteria have been found in the kidney and urine in acute diffuse nephritis, including the staphylococcus, streptococcus, pneumococcus, typhoid bacillus and colon bacillus. The Plasmodium of malaria may be present in the kidney in large numbers.

It is not possible to differentiate clinically between the various sub-types of acute diffuse nephritis. Diagnosis can be made between the diffuse and focal types and these in turn can be differentiated from acute nephrosis. Clinical findings in acute nephritis are characteristic. The condition usually follows immediately on some severe infectious disease or some injury such as extensive burns or exposure to cold. The onset is marked by headache, nausea and vomiting, abdominal pain, gross hematuria, or oedema. The amount of urine is reduced, often to the point of anuria; the specific gravity is low and the lower it is the worse the lesion it indicates. Albumin is always present in small amounts and there is always blood in the urine at some stage. White blood cells are numerous as are all varieties of casts. The blood pressure is always raised at some time in the course of the disease, perhaps for only a day or a week. Oedema is invariable but is usually present. Sodium chloride excretion is good while nitrogen excretion is decreased to varying degrees. The N.P.N. is increased. The water test gives poor results and should not be done. Uraemia is sometimes present. Convulsions may occur, associated with misplacement of water and resultant oedema of the brain.

2. Sub-Acute Nephritis.

If a patient survives an attack of acute nephritis for a period of weeks and begins to improve, the clinician frequently applies the term "sub-acute" to his condition. The term "sub-chronic" may also be used. Six weeks is the period that has been arbitrarily selected; it bears no necessary

relation to change in the kidney condition. Commonly however, at this stage, the kidney tubules are in a state of poor nutrition due to interference with their blood supply by involvement of the glomeruli, and, as a result, the kidney in the gross is pale in color. This is the "white kidney." Usually the cells of the tubular epithelium are swollen and the entire kidney is enlarged in consequence—the "large white kidney" of the earlier writers. Patients in this sub-chronic group cannot concentrate beyond a specific gravity of 1025. There is no polyuria. Albumin is present in varying amounts. Nicturia occurs in the later stages. Red blood cells are seen occasionally and white blood cells commonly. The blood pressure tends to increase gradually. They are subject to oedema due to inability to excrete salt. Nitrogen excretion is adequate.

3. Chronic Nephritis.

A certain percentage of cases of acute diffuse nephritis go on to the chronic state. The percentage is influenced largely by treatment which should be prolonged and the essence of which, is rest. The rapidity with which the end stage is reached depends upon the severity of the primary injury and upon the number of acute exacerbations. The patient may die within six months or live for twenty or thirty years. The average is about eight years.

The cases of chronic nephritis, however, in which a history of a former acute attack is availablefi make up only a small percentage of the total number. In by far the greater number the acute phase has never been recognized. It is assumed that the etiological factors concerned in acute nephritis are also responsible for the development of these chronic cases. The damage being less or the resistance greater, a less acute reaction is produced. The condition is discovered frequently when the individual is applying for life insurance, himself having no knowledge of the existence of the disease. In other cases the patient is an elderly man who finds that he does not sleep as well, or work as well as before, or who feels run down, and the kidney malfunction is shown by urinalysis.

A great deal of work has been done on experimental animals in an attempt to produce kidney lesions resembling those found in man. Many poisons have been used, and with diphtheria toxin and certain uranium salts it has been possible to induce a glomerular lesion which in uranium poisoning is combined with lesions in the convoluted tubules. The animals die however before further changes can be observed. It is not likely that much has been learned to date by this method that will throw any light on the condition in the human kidney.

As in the acute phase, the condition in chronic nephritis has been classified according to the relative prominence of the different structural changes. A glomerular type is mentioned, an interstitial and a parenchymatous. Some writers describe an arteriosclerotic kidney in which lesions are, they believe, the result of primary arteriosclerotic changes in the smaller renal vessels. Other authorities consider this to be the result of peri-vascular inflammation affecting the arterioles and capillaries. It is well to repeat here, that the renal condition found in the generalized arterio-sclerosis is not nephritis and is not a part of the picture of Bright's Disease.

No case of chronic nephritis ever presents a single type of lesion. Instead, all the kidney structures are involved to some extent, though one type of lesion may be outstanding. The picture is that of an organ in which either an insidious process or a repetition of more or less acute attacks has brought about inflammatory and degenerative changes resulting finally in fibrosis, contraction and atrophy. These changes, as they affect the different parts of the kidney, may be described briefly.

a. Glomeruli.—The number of glo-

meruli involved varies—obviously, the greater the number, the more marked will be the encroachment on the functional capacity. The irregularity of the distribution is perhaps explained by the intermittent functioning of the unit, or it may be that different glomeruli have different susceptibilities. Gaskell believes that the sub-capsular glomeruli are most vulnerable and this he considers due to the fact that the vasa afferentes are longer and more liable to damage. The glomeruli affected show varying degrees of fibrosis. Bowman's capsule is usually thickened. There is always a peri-glomerular proliferation of fibrous tissue. Sometimes the tuft becomes adherent to the capsule and the structures fuse into a dense fibrous nodule. Other glomeruli may show sub-acute or acute reactions, with cellular proliferation in the tuft and degeneration or exfoliation. The capsular spaces may contain debris. Occasionally there is atrophy of a tuft with dilatation of the capsule, forming a small cyst.

b. Tubules.—As the glomeruli are involved nutritional changes occur in the tubular epithelium. All stages of degeneration may be seen, the cells appearing swollen, granular or fatty. There may be disintegration and desquamation with collection of debris in the lumina. Frequently the lumina are dilated to form small cysts. In advanced cases most of the tubules may have entirely disappeared. There is always evidence of some regeneration of tubular epithelium.

c. Interstitial Tissue. — The interstitial tissue is always increased in amount. Probably this is partly a reaction to injury and partly an effort at repair or replacement of the destroyed tubules. Mononuclear cells are scattered diffusely through the tissue or localized in small areas here and there.

d. Blood Vessels.—The vasa, the glomerular capillaries and the small arterioles are specially involved. There is proliferation of the capillary endothelium and hyaline changes in the walls. There is also peri-arteritis producing thickening of the walls of the arterioles, involving particularly the media, and occluding the lumina. As a result the entire secretory unit must suffer by reason of interference with its nutrition, and atrophy results. In the blood vessel walls, in the later stages, fatty degeneration of intima and media may be observed.

When large numbers of secretory units are destroyed those remaining undergo hypertrophy in their effort to carry on. While tubular epithelium may regenerate, no new units are ever formed after foetal life; hypertrophy of intact units is, therefore, the only compensatory mechanism.

The gross appearance of the kidney varies. On the one hand there is inflammatory exudation associated with swelling and degeneration in the parenchyma, tending to produce a large kidney, and on the other hand, atrophy and contraction of fibrous tissue tending to make it small. Usually the kidney is large in the early stages, tending to shrink as the condition progresses.

As the process develops the capsule tends to become thickened and adherent to the kidney surface, so that it strips with difficulty. The kidney surface may be coarsely or finely granular, the irregularity being due to hypertrophy of secreting tissue in some areas with contraction of fibrous tissue in others. The frequent occurrence of small cysts in the cortical substance has been mentioned. They contain a clear fluid and often appears just beneath the capsule.

The color of the kidney will depend largely on the amount of blood it contains so that if its blood supply has been interfered with it will probably be pale. Areas of degeneration or scarring are usually yellow or gray. Haemorrhagic areas are red.

The cortex is usually more involved than the medulla and is thickened or thinned according to the stage of the process. Cortical markings are gener-

ally indistinct. Cut ends of blood vessels may be quite prominent depending on the amount of vascular change present and contraction of the surrounding tissue.

Clinical findings in chronic nephritis form no basis for differentiating the type of lesion. In every case the condition is progressive. Obligatory polyuria develops, a state in which the amount of urine is not curtailed by limiting the intake of fluids. The specific gravity becomes fixed at 1012-1014. Albuminuria is less marked than in acute and sub-acute phases. Nicturia is always present. Casts and white blood cells are present in the urine, with occasional red blood cells. The blood pressure is always raised. Oedema does not occur except in an acute exacerbation or when the heart begins to fail under the increased blood pressure. Sodium chloride excretion is barely sufficient and any excess salt is retained. Nitrogen excretion is poor, and sooner or later the products of tissue break-down are retained. The water test shows a fixed output with fixed specific gravity. If the specific gravity becomes fixed at a very low level normal salt and nitrogen concentration in the blood may be maintained for a time by giving excess fluids. When the ability to excrete excess water is lost nitrogen is retained ,and the N.P.N. of the blood is increased. Uraemia develops sooner or later. Retinitis and thirst are commonly present.

For purposes of comparison the clinical signs of a pure arteriosclerotic kidney may be mentioned here. The only constant symptom referable to the urinary system is nicturia. Albumin may be absent. Casts and white blood cells are usually present. The blood pressure is always high. If oedema develops it is due to cardiac insufficiency. Water, salt, and nitrogen excretion are normal.

The pathology of Bright's Disease is thus seen to differ in no essential from that of other conditions. The same phenomena of cloudy swelling and cellular disintegration attend the degenerative lesions of the kidney as are seen in degenerative conditions any where in the body. The inflammations are not different from those occurring elsewhere: there are the same reactions observed of exudation, proliferation and leucocytic infiltration, with fibrosis a prominent feature in the chronic stages. One unusual feature should be noted, namely, that so often the kidney condition progresses to a chronic stage without any antecedent history of an acute attack. This does not mean necessarily that there has been no acute attack. It may mean simply that the reaction has been so slight and the kidney reserve so great that changes in function have not been sufficient to attract attention.

It is further seen that while, in a given case, one part of the secretory unit may be affected more than the others, yet no part of the structure escapes entirely. There is no lesion of the glomerulus without an associated involvement of its tubule, and the reverse is also true. Since the physiology of the kidney is not definitely understood it is not possible to correlate absolutely the pathological and clinical findings; nevertheless much can be learned of the kidney condition from a study of clinical manifestations. Further knowledge may be expected to come to hand as a result of routine observations and specially directed research.

Some of the Common Infections of the Hand *

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In order to diagnose properly infections of the hand accurate knowledge of the anatomy is an absolute necessity. There is never any difficulty in locating the position of the joints, but it is well to remember that they are more distal than they appear; the location of the tendon sheaths of the thumb and fingers however is not so readily kept in mind, so that a brief description of these will be given because they form the pivot upon which so many infections turn.

In the first place it is well to remember that there are no sheaths on the back of the fingers. When a tendon sheath infection is spoken of inflammation of a flexor tendon is meant, and from the practical standpoint no other sheath about the hand is of much importance. Each finger and thumb then has upon its palmar surface a sheath for the flexor tendons. In the case of the index, the middle, and the ring finger, this sheath commences at the base of the distal phalanx and extends for about three-quarters of an inch into the palm. The sheath lies deeply in the finger running close to the bones and joints, particularly to the base of the middle phalanx. The little finger sheath commences in the same place as on the other fingers, but instead of ending in a similar position it suddenly expands into the palm to enclose the superficial and deep flexor tendons of the fingers as well as branches of the median nerve, and then proceeds upwards beneath the anterior annular ligament to a distance of an inch or more above the ligament and in close apposition to the pronator quadratus muscle. The sheath for the thumb likewise commences just beyond the terminal joint, and lies close to the proximal phalanx, but then turns away from the metacarpal and the under surface of the anterior annular ligament and reaches a position on the outer side of the sheath of the little finger, with which there is a communication in a large percentage of cases.

There is a further anatomical point to keep in mind, namely that between the tendons in the palm and the metacarpal bones with their interossei muscles there is a more or less closed space which is open towards the fingers, and it is into this potential cavity that infection so often enters forming a palmar abscess. One further observation upon the aantomy, the lymphatics of both fingers and palm travel towards the dorsum which explains why the maximum swelling is so commonly seen on the back.

Infections of the hand usually follow some form of traumatism either trivial or severe, although they may arise from a blood borne cause. Many of them are confined to the terminal phalanx and this group comprises the ordinary felon, infections of the subcutaneous tissue and paronychia. Infections occur at different levels here as elsewhere, so that there may be an inflammation in the subcuticular area only, in which instance blisters will form which quickly become purulent. If the seat of the trouble is immediately beneath the skin a localized cellulitis results, while in the true felon the infection commences beneath the periosteum. Clinically these latter groups can not be differentiated, for in each there is a swelling limited to the terminal phalanx accompanied by pain of a throbbing character, which will prevent the sufferer from sleeping. The treatment in each case is the same, an immediate incision into the most tender area to one side, which should stop as soon as pus has been found. In neglected cases the whole diaphysis of the

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phalanx may separate as a slough. A paronychia or as it is commonly called "a run around" starts underneath the lateral edge of the nail, in the great majority of instances there is no hang-nail or history of injury. It tends rapidly to extend beneath the base of the nail to the opposite side. The picture is characteristic in that the skin adjacent to the nail is red, swollen and tender. The treatment consists in insinuating the flat end of an ordinary probe under the lateral edge of the nail, when pus will invariably be evacuated. In some cases this will suffice to produce a cure, but in the majority of instances it is necessary to remove the whole of the base of the nail. In neglected cases it is common to see exuberant granulation tissue springing from behind the base of the nail in the midline.

Furuncles are fairly common in the hand, particularly over the dorsum of the proximal phalanx where hairs are common. The indurated area is well localized, although there may be much œdema on the dorsum of the hand, and movement of the affected finger will be painful. A crucial incision to relieve the tension, followed by intermittent moist heat is the most appropriate treatment. As soon as the slough has been removed cicatrization rapidly follows.

The second group of infections—those involving suppuration in the tendon sheaths—is a much more important variety, and is the type that frequently is undiagnosed. The sheath may become involved in open wounds or secondarily to an infective focus in the neighbourhood, but this latter is certainly rare. In the vast majority of the instances that one sees, there has been a quite insignificant pin prick on the front of the finger or a small sliver has penetrated a short distance beneath the skin. Then within a few hours or days, depending on the length of time the streptococci take to get by way of the lymphatics to the sheath, the finger becomes intensely painful and rest is impossible. At this early stage there may be no redness of the finger at all, but there is always some swelling and usually this is greatest on the dorsum of the finger, and later on the back of the hand. If the middle finger be the one affected, it will be moderately flexed and if there is much swelling, then the other fingers will be flexed as well.

To diagnose a tendon sheath infection of the middle finger—and the same applies to the ring and index fingers—there should be four causes of exquisite or excruciating pain, and these are produced by (1) straightening the finger; (2) pressure over the front of the middle phalanx; (3) pressure over the front of the proximal phalanx, and (4) pressure over the front of the head of the metacarpal.

Very frequently these cases are incorrectly diagnosed. The reason, I believe, is that we fail to make a proper examination. In the first place it is necessary to form a proper opinion of the individual's response to pain. This is done by palpating œdematous areas, for example, the back of the hand. These will undoubtedly be tender, but are not exquisitely so in normal individuals. Do the same to the back of the finger affected, taking particular care that you do not put any pressure upon the front. In this way palpate the middle and proximal phalanges and their joints on their dorsal aspect. If carried out carefully no pain which makes the patient wince will be produced.

Now extend in turn the unaffected fingers. Pain, varying with the sensitivity of the individual, will probably be experienced, but not of the exquisite variety and is due most likely to the œdema in neighbouring structures.

Now carry out the four tests outlined above, and in each instance excruciating pain will be produced. Pressure upon the three points in front is applied by a finger and humb to the front and back respectively, and therefore it is necessary to be sure that the pain

is not caused by the dorsal pressure which has been ruled out by the preliminary investigation of the back of the finger. It may happen that when seen the pain is not nearly so severe as previously. This may be due to the tension having been relieved by rupture of the sheath, which occurs at the proximal end into the palmar space between the tendons and the metacarpal bones. In addition to the local signs which are all important, there will be the usual accompaniments of malaise, fever, a leucocytosis and acceleration of the pulse rate.

The treatment of a tendon sheath infection is immediate incision, and always under general anæsthesia, and with a broad tourniquet applied upon the arm to assure a bloodless field. The great essential is to establish free drainage and prevent the spread of the infection to the palm. Two incisions usualy suffice—one on the side of the middle phalanx, the other on the opposite side of the proximal phalanx, and extend this incision about half an inch into the palm. If there is already a deep palmar abscess when first seen, as evidenced by exquisite pain and swelling proximal to the limits of the sheath, then push a pair of closed artery forceps beneath the tendon and to the side of the most marked palmar pain, and deep enough to feel the front of the metacarpal bones, and open them, when the pus will surely be evacuated. An elastic band is inserted to ensure patency of the passage. Some surgeons prefer one long incision in draining such sheaths. The objection is that the tendons will likely protrude from the sheath, but on the other hand it provides the best drainage. When you consider that in practically all instances all movement at the distal and proximal interphalangeal joints is permanently lost, it probably doesn't matter much whether the tendon sloughs or not.

If one can diagnose an infection in a middle finger tendon sheath an infection of the little finger should not offer any obstacle. Besides the four signs indicated, there are the exquisite points of tenderness along the ulnar side of the palm and above the anterior annular ligament. Flexion of the thumb is to be expected because of the close association of the sheaths under the anterior annular ligament.

In treating a little finger sheath instead of stopping about half an inch above the webb of the finger the incision should be carried upwards as far as the lower border of the anterior annular ligament. A second incision should then be made in front of the lower end of the ulna keeping close to its anterior surface. When through the deep fascia by blunt dissection, push a pair of forceps under the tendons and vessels and close to the ulna and radius and the pronator quadratus, until pus is found. A rubber drain is then inserted.

Suppuration in the flexor sheath of the thumb will have exquisite tenderness in front of the proximal phalanx, to the inner edge of the thenar eminence and again above the anterior annular ligament. If the infection travels across from one side to the other, then a combination of little finger and thumb sheath infection is the result.

The treatment of thumb sheath is very similar to that for the little finger, except that the incision which opens the sheath in front of the proximal phalanx must not be carried up farther than half an inch distal to the lower border of the anterior annular ligament, which is about the size of a two cent stamp, otherwise the branch of the median nerve to the thenar muscles will be severed, as this nerve crosses superficial to the tendon.

The next important group of hand infections is that commonly called cellulitis. It is divided into two classes—superfiicial and deep, the former being located in the superficial facia while the latter is beneath the deep fascia. The former variety is by far the commoner type, and is usually caused by slight injuries such as abrasions or

slight cuts. The deep variety is sometimes a sequel to the superficial, or it may complicate a deep wound from whatsoever source.

There are three varieties of superficial cellulitis: (1) Mild cases which clear up without suppuration; (2) cases complicated by suppuration, and (3) those in which there is no pus formation, but in which there is septicæmia.

The mild cases are the most frequent, and are characterized by swelling, redness, tenderness and pain in the affected part, together with mild evidences of a toxæmia. Red streaks will likely be seen running either to the epitrochlear or axillary glands. If it is a finger which is involved there will be generalized tenderness, and movement of the finger will be painful because of the associated œdema in the joints and sheaths but there will be no exquisite tenderness in the four areas as in sheath infection. In most instances there will be enlargement with pain of the epitrochlear or axillary group of glands. In a few days all signs and symptoms will have subsided.

In the second group there are many different degrees of suppuration, varying from the single small abscess in the subcutaneous tissue to such a complete destruction of the hand that amputation is required. In this group the onset may be no more abrupt than in the first group, but the patient's resistance, whatever that means, is below par, and the bacteria run riot with extensive local destruction. There is always great swelling on the dorsum, and in extensive cases on the back of the fore arm, where abscesses frequently form. In very severe cases large areas of skin on the back become gangrenous. In still other types there is an associated tendon sheath infection followed by a deep palmar abscess, or there may be bone and joint involvement. At other times a small focus in the hand is quickly followed by a deep abscess in the forearm; while again it is not rare to see a trivial cellulitis in a finger followed a fortnight or more later by an axillary abscess.

In the third group, fortunately rare, the onset is sudden and within a few hours the individual is profoundly ill. A severe chill is often the first indication, and while the hand and forearm are quite badly swollen and great œdema is present on the dorsum, yet no pus formation occurs. There is little or no glandular involvement either in the epitrochlear or axillary regions, and the red streaks of lymphatic involvement are absent. There is in fact a septicæmia to which the patient quickly succumbs.

Arthritis and osteomyelitis, often associated in finger and hand infections, may be primary conditions, especially in wounds which directly open a joint, in which case the diagnosis is obvious from the pain, swelling and tenderness being located at the joint line. But they are common sequelæ to long standing inflammation originating as a cellulitis or tenosynovitis and when the discharging sinuses are examined we find necrosed bone.

A common form of suppuration seen in the hands of laborers is an abscess in front of one of the heads of the metacarpals. The history is that of blister formation followed by the signs of inflammation. On examination the adjacent areas are tender, and it will be found that pressure over the centre causes very severe pain. It is cured by a short vertical incision which must penetrate the palmar fascia since the purulent collection in these cases lies between the flexor tendon sheath and that structure.

The treatment of cellulitis as far as operative measures are concerned is particularly simple viz., open abscesses when they form. The old plan, still used by some, of making multiple incisions, not only does no good, but actually does harm. Apart from draining abscesses our sheet anchor is intermittent moist heat, and this applies to all varieties of hand infections where there

are no pent up pockets of pus. The hand is placed in a bath containing hot saline with boracic acid, and left there for an hour after which it is removed and wrapped in dry sterile gauze for two hours, when the bath is again employed. This routine is kept up during the day and once at night if the patient be awake, until the active process has subsided. No other local measures are necessary. In addition the general health must be supported by nourishing easily digested food, and excretion of toxins aided by elimination.

In all infections of the fingers and hand where there is the possibility of resulting deformity it is very important to see that the parts are kept in that position in which the greatest usefulness will ensue. For example, if there is only slight movement left in the fingers it will be infinitely better to have them in a partially flexed position so that they can be approximated to the thumb than to leave them completely extended. Again, if fixation of the wrist is feared from extensive carpal involvement, then the hand must be kept dorso-flexed, else a very weak hand will result.

If there is a joint involvement, grating will be felt on passively moving one bone upon the other. As to treatment, certain general principles apply. All sequestra should be removed and conservatism should be the watchword when dealing with the thumb; the little finger is the least useful of all. If either arthritis or osteomylitis of a finger is associated with a tendon sheath infection then amputation is the only procedure except in the thumb, since almost any kind of a thumb is infinitely better than none. At times a shortened finger can be obtained after sequestrectomy with a surprisingly good function.

Admittedly, the diagnosis of infections of the hand is difficult, and mistakes are of serious import to the patient. But again we repeat that most failures are due to hasty and improper methods of examination. The recognition and proper appreciation of tenderness on pressure is the real basis of success. It is not sufficient that the patient says a certain area is tender; the surgeon must satisfy himself that real tenderness is present, and not be misled by the tenderness which is so common an accompaniment of œdematous areas, otherwise he will be making incisions which are not only useless, but positively harmful.

Protein Sensitization.

A Discussion of Various Concepts, by Cecile Cohen, 2T9.

Although the present conceptions of allergy and protein sensitization have arisen chiefly in the last twenty-five years, the first clinical observation was made by Jenner in 1798, when variolous matter was injected into a woman who had had cowpox 31 years before "an efflorescence of a palish red colour" appeared quite suddenly about the site of injection. One hundred years later Hericourt and Richet discovered that repeated injections of eel serum into dogs gave rise to an increased susceptibility to this substance and they coined the word anaphylaxis, meaning "without protection," to name this phenomenon.

The nomenclature in this field is confusing. Kolmer suggests that the term allergy be used to include all the phenomena of hypersusceptibility; that the term hypersensitiveness be used when the exciting agents are non-protein substances, and anaphylaxis where the exciting agent is a protein or protein derivative.

In general, anaphylaxis is considered to be an antigen-antibody reaction taking place in the cells of the body, as is shown by Dale's demonstration of anaphylaxis in the excised uterus of a sensitized guineapig. An innocuous amount of protein antigen called the anaphylactogen or sensitinogen, when injected parenterally, causes the formation of antibodies by the body cells. This is called active sensitization and at least 6, usually 8-10 days must elapse between the original or sensitizing dose and the intoxicating dose. The antibody is in two situations. Part, the sessible antibody, is attached in some way to the tissue cells, which are thus sensitized, and remains there until free antigen is brought in contact with them, causing anaphylactic shock. The rest is free antibody and remains for some time in the blood. The amount of free antibody varies with the size and spacing of the early injections and there is evidence to show that these antibodies are identical with precipitins. The fact that Richard Weil passively and actively sensitized guinea pigs, using the precipitate that resulted from mixing antigen and antibody is evidence for the existence of free antibodies and their identity with precipitins.

In animals even when so few antibodies are present that precipitation can not be obtained, it is possible by introducing the blood or serum of a sensitive animal into a normal animal that the latter will react to the first injection of the antigen. This is called passive sentitization and it too has a latent period, but only minutes or hours instead of days need elapse between the sensitizing injection of serum and the intoxicating injection.

Desensitization usually means a gradual saturation of the fixed antibodies with antigen as can be demonstrated in smooth muscle preparations as well as in the living animal. When the animal recovers from anaphylactic shock it is said to be desensitized, that is, it will not react to a similar injection of the same substance. This fact is of fundamental importance.

The symptoms and pathology of anaphylaxis vary considerably in different animals but in any species they are the same for all antigens.

In man—fatal anaphylaxis is fortunately rare and only follows the administration of horse serum to "horse asthma" subjects. The usual reaction following an injection of serum is an immediate attack with or without the later development of serum sickness some days later. The essential anaphylactic lesion is apparently contraction of smooth muscle followed by relaxation. For this reason dilation of vessels accompanied by serous exudation, are found and cause the characteristic joint and skin lesions especially the urticaria seen in allergic conditions. The exanthemata of some acute infectious diseases may well be of anaphylactic origin.

The guinea pig is the animal most often used in experimental investigations. It is easily sensitized in 10-16 days by a single minute injection of protein and remains sensitive for months or years. The intoxicating dose may be given intravenously, subcutaneously or intraperitoneally, and in a few seconds or minutes, depending upon the dose and route, the animal becomes restless, respiration is embarrassed, it scratches its nose, breathing is spasmodic, the guinea pig becomes agitated and there is discharge of urine and faeces. The exhilaration is followed by weakness, the animal falls on its side, quite limp. There are usually a few convulsive movements, then death. It may recover at any stage up to actual death. All this may take place quite rapidly or may last an hour.

At autopsy the most striking changes are in the lungs, which not only remain fully distended but the walls of some alveoli may be upturned. The bronchi, due to the smooth muscle in the walls, are so tightly contracted that squeezing the lung between the fingers ruptures the alveoli instead of dilating the bron-

chi. The heart beats after respiration ceases. Neltzer suggested on the basis of the post mortem findings in such guinea pigs that clinical asthma is the result of foreign protein sensitization. Anaphylactic shock in rabbits is characterized by myocardial failure, then prostration and lastly excitability. The lungs collapse and the pulmonary circulation is obstructed by spasm of the musculature of the pulmonary arterioles. In dogs the predominant feature is hepatic congestion with fall in blood pressure. The contraction of smooth muscle is the characteristic lesion of anaphylaxis.

Certain criteria for true anaphylaxis have been formulated by H. Gideon Wells.

1. The observed toxicity of the injected material must depend upon the sensitization of the animal, i.e., the substance must not produce similar symptoms in non-sensitized animals.

2. The symptoms produced must be those characteristic for the species under study.

3. It should be possible to demonstrate passive sensitization with the serum of sensitized animals.

4. It should be possible to demonstrate amelioration or prevention of the bronchial spasm in guinea pigs by proper use of atropin and epinephrin.

5. The possibility of the symptoms being caused by thrombosis or embolism must be excluded. This group of reactions are termed anaphylactoid or sometimes colloid shock. They are caused by intravenous injections of serum acted on by agar, insulin, starch, etc. Peptone produced symptoms more nearly like anaphylaxis, but there is greater tendency for thrombosis, hemorrhage and oedema of the lungs.

6. After recovery from anaphylactic shock there should be exhibited a condition of desensitization under proper conditions.

Several problems with regard to antigens require investigation.

Practically any soluble protein will produce sensitization and intoxication of susceptible animals if it is foreign to the blood of the injected animal. The commonest proteins are sera, foods, effluvea of animals, pollens and bacteria and their products. The specificity of the reaction seems to depend on the chemical structure of the protein molecule rather than on its biological relationship. Wells showed that chemically similar proteins from different grain react anaphylactically with one another while chemically dissimilar proteins from the same source fail to do so. The slightest impurity in a protein can be detected by this method even if the foreign protein be present in 1 part in 100,000. It is for instance quite possible to detect adulteration of sausage with horse meat in this way.

It has been known for a long time that guinea pigs could be sensitized via the gastro-intestinal route, but it is only recently that Ratner, Jackson and Gruehl sensitized them by spraying horse dandruff into the cages. A subsequent injection of horse dandruff killed the animals in typical anaphylactic shock while in others further spraying caused symptoms comparable to those in human asthma. Food by mouth can also sensitize, but in the human this problem is complicated by the fact that if a large amount of one protein be taken it may pass into the circulation through a normal mucous membrane.

Allergy to non-protein substances, of which quinine intolerance may be cited as an example, presents one of the most perplexing problems in immunology. Apparently the phenomenon is not confined to the human race as for example the intolerance of cattle to mercury, also salvarsan. Sometimes animals and humans react to drugs with which they have no history of previous contact. One theory accounting for this type of sensitization is that of Wolff Eisner who believes that drugs may combine with serum or tissue proteins, especially the skin, and form a protein sufficiently foreign to act as a sensitinogen.

The most important groups of these non-protein antigens are:

1. Glucosides of various plans—Rhus toxicodendron.
2. Alkaloids from opium, quinine bark, belladonna, etc.
3. Essential oils and balsams—cubiles, sandalwood, resins, turpentine.
4. Metals—Mercury arsenic.
5. Halogens—Bromides and iodides.
6. Coal tar, benzol and melbune derivatives — Antipyren, salicylic acid, creosote, salol, etc.

Although repeated attempts have been made it has not been possible to passively sensitize animals with the sera of drug sensitive individuals.

The mechanism of the production of anaphylaxis is still controversial but it is established that the site of the reaction is a cellular one. To prove this Block grafted sensitized skin on a normal individual and found that it remained sensitive. The classical proof was elaborated by Dale using the Schultz Dale technique. A virgin guinea pig of about 300 grams that had been sensitized three weeks previously was killed and the uterus perfused with Giner Locke solution for several hours until all the serum was washed out. One horn of the uterus was then suspended in oxyginated R-L solution and attached to lever and recording drum. When the specific antigen was added the uterus contracted immediately. After some minutes it relaxed and the addition of further doses of antigen caused no further contraction — although the uterine muscle was not fatigued as it responded briskly to histamine or pituitrin. It was also possible to resensitize the muscle by prolonged contact with (immune) serum of high antibody content.

Other facts indicating that the reaction is cellular rather than humoral are (1) it takes place so rapidly that no known forment could break down protein in the time available.

(2) Weil exanguinated and transfused animals at the height of the anaphylactic attack and found that the normal recipient of the anaphylactic blood remained normal while death resulted in the sensitized animal although transfused with normal blood.

The mechanism of the reaction, so Dale, Kolmer and others believe, can be accounted for by the antibody bearing such a relation to the antigen that when they meet a disturbance of the condition of colloidal equilibrium is set up in the sensitized cells. Probably all the cells are sentisitized although the reaction is more apparent in the smooth muscle cells that contract. Another view is: In the intracellular antigen—antibody reaction histamine, which normally can be extracted from the tissues, is liberated and acts on the muscle, nerves and blood vessels causing the syndrome seen in anaphylactic shock. This theory is very attractive in view of the similarity of symptoms produced by both—contraction of smooth muscle, increased capillary permeability, fall in blood pressure in dogs, similar urticarial reactions, etc

The two facts against this view are: histamine does not lower body temperature nor does it influence the coagulability of the blood. Of course it is possible that these effects in anaphylaxis may be due to other substances.

It is more difficult to correlate the phenomena found in man with those of the lower animals because it is usually impossible to sensitize guinea pigs passively with human serum. Coca recently reported that sensitization to ragweed was produced in one monkey by injecting 50 cc. of serum from ragweed sensitive humans. Negative results were obtained in three other monkeys and in chimponezes. Schloss and Larsen have reported sensitization with the sera of infants sensitive to cow's milk and other foods. Ramirez reported that a man who had never had hay-fever, asthma or urticaria received a transfusion of 600 cc. of blood. Two weeks later the patient went for a carriage ride and in five minutes had a typical attack of asthma. A skin test yielded a positive with a 1/20,000 dilution of

horse dandruff but not to other proteins.

Recently an important development has occurred in this field—namely, local passive transfer of sensitization. Although transference of sensitiveness from man to animal is difficult it is easy to confer local skin sensitiveness on a normal individual by an intradermal injection of a small amount of serum from a sensitive individual. The more active his skin reaction is, regardless of how mild the disease is, the more active will be his serum and if very active it may be diluted a thousand times before injection and still confer local sensitization. Next day a small amount of the offending protein is injected intradermally into the area marked, or a scratch is made and a minute quantity of the protein and a dilution of protein solution put on it, and within a few minutes a positive reaction with formation of an urticarial wheal and erythema is seen. One application will desensitize to subsequent applications of the same solution.

Local passive transfer is of use clinically in cases where the trauma of scratch or injection produces a skin reaction in the patient that will mask the reaction of the specific protein. The Berkfelded serum of the patient is injected intradermally into 20 or more areas in the skin of a suitable normal. It has been found that 85-90% of people are suitable for desensitization by this means. A day or more after injection the marked sites are tested with the suspected proteins and the results recorded.

One is inclined to stress the similarity of anaphylaxis and human sensitization. Coca however believes that allergy is not fundamentally an antigen-antibody reaction but is dependent upon an allergic state, acquired largely by inheritance, a state that is present in some individuals but not in others. It is futile to attempt to discuss this matter at further length except to mention the important work of Avery and Heidelberger, who have shown that polysaccharides may endow bacterial antigens with some of their specific properties and that although these polysaccharides do not produce antibodies when injected into animals they will act as antigens and give precipitin reactions when brought in contact with the serum of animals immunized with the whole bacteria.

It may be of interest to discuss a few conditions that may or may not be of allergic origin. In Status Lymphaticus, Delafield and Prudden, suggest that anaphylaxis might be the cause of death—the body being sensitized by a specific nucleo-protein formed in the lymph nodes as a result of necrosis of the germinal follicles. The tissues on subsequent injury may give rise to free antigen, thus causing anaphylactic shock. Sympathetic opthalmia is probably a manifestation of hypersensitiveness as are also intermittent hydrathrosis, erythema mulliforme, lenticular cataract and the definitely recognized entities of asthma urticaria, etc.

It has seemed possible to me that the reason tissue grafts do not take, especially homologus as distinguished from autogenous, is because of an active sensitization to the foreign protein. The graft usually lives but does not grow. At the end of one or more weeks the body cells now being sensitized—the protein is still being absorbed and a reaction occurs followed by sloughing of the graft.

We may expect from the present outlook that in the not distant future science will be able to throw light on this most interesting subject.

Acute Appendicitis *

R. H. Meredith.

The first case of appendicitis on record was operated on and reported by a French surgeon, Mestiver, in 1759, and although the pathological condition was well described at autopsy, it made no impression whatever on the conduct of such cases. In 1812 Parkinson, the well-known neurologist, reported the first case in the English literature. The year 1866 marks a turning point in the consideration of morbid conditions in the right iliac fossa. Prior to this year many different abdominal disorders localizing in the right iliac fossa were variously termed typhlitis, peritphlitis, caecitis, etc. At this time Reginald Fitz, a Boston surgeon, coined the word "appendicitis." His comprehensive review of the literature and clear report of a large number of cases in his own practice, practically inaugurated a new school of thought concerning conditions in the right iliac fossa. His excellent work prepared the way for our present day understanding of appendicitis. In England it was not until 1901 that appendicitis became a separately notifiable and recorded cause of death. This was about the time of the historic operation on King Edward VII for appendicular abscess on the eve of his coronation.

Appendicitis is essentially a disease of young adult life. However, no time of life from infancy to old age is exempt. Anderson reports a case of appendicitis operated on successfully in a woman of eighty-eight years. The earliest authentic case was operated on by Gloniger in an infant only forty-one hours old, in which the baby made a good recovery. Slightly over a year ago there was a newspaper account of an appendectomy performed at the Detroit Receiving Hospital on a baby one hour old. An age incidence has been constructed from the findings of Bolling, Kelley, Churchman and Sargent as follows:

Age			Cases
Under 5 years		.....	1-3%
5-10	"	.....	8.5%
10-15	"	.....	16. %
15-20	"	.....	24. %
20-30	"	.....	40. %
Over 30	"	.....	8-10%

There is no obvious reason, anatomical or pathological, why the disease should occur more frequently in one sex than in the other, yet it is found that the preponderance in males is 1:1.

When a disease leaps into extreme prominence within two or three decades, becomes an everyday finding in the hospitals of certain more civilized countries and leaves the rest of the world alone, surely the riddle of its causation should not be hard to solve, yet it has proved so. The distribution is peculiar and it presents an important etiological factor. In Holland the death rate from appendicitis is high, yet in Denmark close by it is low. The essential difference between the two peoples is a dietary one. In the latter much less meat is eaten than in the former. In Italy and Spain the disease is rare. Here again meat forms a small part of the diet and their foods are well lubricated in olive oil. The peasants of Roumania seldom have appendicitis yet it is fairly common in the cities. Here again the salient point is that the peasantry subsist chiefly on vegetables. In England, Canada and the United States the disease is very common. The modern diet in these countries is well known to be high in proteins. In the West Indies the blacks predominate by 12:1 over the whites, yet the cases of appendicitis almost always occur in the white population. The black children

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are brought up on sugar and water whereas the white children are brought up on milk. In China it is quite rare. Gibson reports that in Hong Kong in the last thirty-seven years there have only been reported ninety-three cases. It is interesting to note that cases of acute appendicitis in the Chinese usually result in death, since they consider operation a last resort. Also opium is freely given which masks the severity of the condition. The principle ingredients in the Chinese diet are rice and vegetables. In Persia all food is cooked in grease and appendicitis is rare. Appendicitis is quite uncommon in poverty-stricken southern Europe. Inmates of prisons, work-houses, and poor homes are infrequently victims of appendicitis. In these circumstances the diet is simple, vegetables being the chief constituent. Experimentally it has been shown that rabbits fed on a cellulose-free diet develops an inflammation of the caecum.

On the other hand, one may consider the Eskimos who live chiefly on raw meats with few vegetables and fruits, and yet among these people appendicitis is rare.

McCarrison believes that the freedom of native Himalayans from ulcer, appendicitis and cholecystitis is referable to their diet. Moffit criticzes this statement, and says that it can equally well be attributed to their freedom from infection, and freedom from the nervous strain of modern urban life.

Nevertheless, it would appear to be true, that where the diet is composed chiefly of cellulose-containing vegetables the incidence of appendicitis is low while where the diet is a modern high protein one the incidence is high. It has been observed that natives, who forsake their own diet for a modern one, become subject to appendicitis.

Diet and constipation are intimately linked with one another. Kelly states that 50% of cases of appendicitis give a history of previous constipation. This number is probably small because of the relatively large number of persons whose bowels are regular but who are still found to be constipted. Hurst definitely states that chronic constipation may lead to appendicitis. A history of indiscretions of diet is often found in cases of appendicitis.

The actual bacterial organisms responsible for the acute appendic are not numerous. B. Coli Communis is considered the most common etiological agent by Kelly and Deaver. It is a commonly accepted theory that duodental catarrh may obstruct the common bile duct, and thus it may be assumed that catarrh of the caecum may cause obstruction of the appendix. The secretion of mucus, and fecal matter are thus essentially retained in the appendix. Russel claims that this favorable nidus for growth raises the virulence of the ever present B. Coli. While most writers agree that B. Coli is the most common causative agent its importance is not so well assured. Strep. Pyogenes can be isolated in only a minority of cases of appendicitis. Nevertheless it must be considered as of the greatest importance etiologically in the causation of the disease. It is associated with all cases of very severe infection and is the usual cause of extensive and rapidly fatal peritonitis. It is difficult to cultivate and is often overgrawn by the other organisms present in the intestinal tract. There is no doubt that B. Coli is the commonest secondary invader in all cases of appendicitis. Staphylococcus is not uncommonly a cause. It rarely causes general peritonitis, usually confining its pathological activities to the peri-appendicular tissues.

Pneumococcus rarely causes appendicitis. B. Lactis Aerogenes, B. Pyocyancus and B. Proteins Vulgaris, found normally in the intestinal tract, rarely causes appendicitis and then probably only as a secondary cause. The commonest parasitic cause is Oxyuris Vermicularis. Some authors deny this and state they are only present secondarily and quote cases with pin worms in the appendix in the absence of appendicitis. However these two views may not be

incompatible, and when one finds a patient with the classical picture of appendicitis and at operation finds an appendix filled with pin worms with no other obvious pathology, it is reasonable to presume that they are the causative agents. Certainly they rarely cause gangrene of the appendix. The rarity of appendicitis under two years of age might be explained to a slight degree by the fact that parasites are uncommon at such an early age. Foreign bodies as seeds, fish bones, gall stones, etc., probably only play a subsidiary role in the causation of acute appendicitis. Trauma is more commonly an etiological factor than is generally supposed.

Menstruation would seem to be a factor according to Kelly, who claims that the splanchnic congestion due to the lowered peripheral blood pressure favors the production of appendicitis. The preponderance of the disease in males does not add support to this theory.

There seems to be some association between appendicitis and rheumatic fever, and also with Influenza.

Abnormal situation of the appendix is an important factor at times in the causation of appendicitis. Sir Frederick Treves has stated "the only constant thing about its position is its inconstancy." The appendix may come in contact with many abdominal organs. Ochsner states that 35% of cases of cholecystitis have an associated appendicitis. Other authorities stress the frequency of associated salpingitis and appendicitis.

Both from England and the United States have come alarmist reports on the great increase in appendicitis with the resultant criticism of our modern treatment. Since appendicitis is not a notifiable disease it is very difficult to arrive at any accurate morbidity rates but from clinical experiences over the last half century one would probably be safe in assuming that the incidence has doubled every ten or fifteen years. Now if one turns to the mortality rates for the last twenty-seven years he finds little or no increase and thus it would seem that the treatment has kept pace with the rising incidence so that the death rate has remained stationary.

While the death rate from appendicitis is not greatly on the increase, one must not forget that it is a serious cause of death. Willis states that the annual toll taken by appendicitis almost equals the combined total of intestinal obstruction, gall-stones, gastric and duodenal ulcer. The significance of this statement is more impressive when one realizes that this number is taken from the most valuable of our population.

In many cases of appendicitis the clinical history is so typical that the diagnosis is relatively simple, yet in many others it is painfully difficult. This latter is realized when we think of the statement of R. F. O'Neill that 25% of patients with ureteral calculi had had an appendectomy performed. The signs and symptoms of a typical case are thus laid down by Cope:

1. History is usually exposure to cold, dietary indiscretions or general abdominal symptoms. Early diarrhoea or constipation are common.

2. Signs and symptoms: The diagnostic feature is pain or "indigestion," beginning in the epigastrium and in two hours spreading over the whole abdomen and, in six to twelve hours from the onset, localizing in the lower right quadrant. Rawls claims that this occurs in 70% of cases. Nausea, vomiting and anorexia occur early, usually a few hours after the onset of the pain. Deep tenderness occurs from the first but is masked by the initial pains. This is most constantly found just below the mid point of a line joining the anterior superior spine to the umbilicus. Local hyperaesthesia is commonly found, most frequently in an area one inch to the right of the umbilicus and on a level with it. Local muscular rigidity in a large proportion of cases is not present as an early symptom. When the appendix is situated in the pelvis this rigidity may never be detected. It

varies considerably, three degrees being described, the first shows only a slight rigidity on deep palpation, the second occurs as a stiffening as soon as the hand touches the skin, the third presents a persistent board-like rigidity which does not move on respiration. Rigidity of the psoas muscle should be tested by hyperextension of the thigh when the patient is lying on the left side. Rigidity of the obturator internus is also noted by internal rotation of the flexed thigh. Rigidity of the quadratus lumborum may be detected by pressing forward below the costal margin in the scapular line. Iliescu stresses the value of the new sign in appendicitis. He states that pressure on the right phrenic nerve in the middle of the triangle formed by the two heads of the right sternomastoideus and the clavicle causes pain, and he claims this to be due to an ascending right lymphangitis, causing irritation of the phrenic nerve on that side. Fever shows a gradual increase in the first twenty-four hours. The pulse is often normal, persistent acceleration meaning peritonitis. Gibson gives the average leucocyte count at 18,000 with polymorphs 84%.

3. Order of occurrence of symptoms is commonly as follows: (a) pain, (b) nausea and vomiting, (c) local iliac tenderness (rectal or otherwise), (d) fever, and (e) leucocytosis.

Notable cases present so definite a clinical picture. Pain is usually present but may occasionally be absent. It may often begin in the right iliac fossa. Pain once present but suddenly disappearing is not a good sign and may indicate gangrene of the appendix, the reflex arc having been destroyed. Nausea and vomiting may be absent, but if present the occurrence is always following the onset of pain. If nausea and vomiting with fever are present before the pain then the condition is not appendicitis. Local iliac tenderness is usually present. Marlow tells us that spasm of the pylorus is often present in appendicitis and a point of tenderness may be found in the pyloric region. This may be confusing and cause some to miss the more pronounced area of tenderness lower down. The temperature may be normal or even subnormal in either mild or severe cases. The pulse usually follows the temperature in typical cases but of all the clinical signs and symptoms, pulse and temperature are probably of the least value. A disagreement between pulse and temperature is a bad sign, applying either to high temperature and low pulse or vice versa. The local signs may be absent or poorly defined but the appearance of restlessness, pinched facies, disagreement between pulse and temperature, and abdominal distension, all indicate a dangerous attack. Urinary symptoms occur often, especially when the appendix is situated in the pelvis.

In children the diagnosis is complicated, since they cannot clearly define symptoms or accurately localize pain, and also by the fact that the classical picture is presented by other commonly occurring conditions. Pain may be low down due to the relatively long appendix in children. Nausea and vomiting in children before puberty are not reliable for diagnosis. The examination of the acute abdomen in a child is an ordeal for all concerned. The child is apt to cry when touched anywhere and the abdomen is held as rigidly as possible. Hence tenderness in a fretful child is difficult to interpret. Rectal examination is very important in children as the pelvis is so shallow. Hence urinary symptoms are apt to predominate.

The differential diagnosis includes many conditions which will be considered briefly in groups.

1. Pelvic Inflammatory Disease: This includes salpingitis, ruptured ectopic, ovarian cyst with a twisted pedicle, and red degeneration of a fibroid. These can usually be eliminated by a careful history and pelvic examination, but the possibility of an acute

appendicitis associated with any of these conditions should not be overlooked.

2. Renal Disease: Pyelitis has a higher temperature and an initial rigor. Examination of the urine should help in the differentiation. Stone may often be ruled out by the absence of fever and constipation and by a careful history.

3. Gastro-intestinal Disease: Ulcers and malignancy, with or without perforation may simulate appendicitis. These with cholecystitis can usually be ruled out by a careful history. Goldie says that a diagnosis can nearly always be made on such cases if one takes an hour to obtain an intelligent history. Gastro-enteritis in children must be excluded. Usually there is a history of dietary indiscretion, relieved by vomiting. There is usually no marked fever or leucocytosis. Intususception is ruled out by the history and rectal examination.

4. Pneumonia: This is important to differentiate at any age. Due to the rarity of appendicitis in young children, and the frequency of pneumonia, and the fact that in both there may be fever, nausea, and vomiting, leucocytosis, abdominal pain and tenderness, much confusion results. In pneumonia the patient is flushed, restless and breathes with the diaphragm. In appendicitis he is pale, docile and keeps the abdomen quiet. Parker states that with the above symptoms, if the respiratory rate is more than one-third the pulse rate the cause is probably intrathoracic, and vice versa.

The most important complications of appendicitis are considered briefly as follows:

1. General Peritonitis: This is the most critical accompaniment of the early stages of the disease and is the usual cause of death.

2. Intestinal obstruction due to paralytic ileus is usually a post-operative complication in ruptured appendix and may occur early or late. It is stated to be absent in children by Bolling.

3. Pylephlebitis is comparatively rare.

4. Subphrenic abscess. The usual history is of a patient coming in six weeks after operation for ruptured appendix with fever, leucocytosis, pain and tenderness in the right upper quadrant, with positive X-ray findings of a high diaphragm and a mass below the diaphragm. There is often an air bubble between the diaphragm and the dome of the liver. Oedema of the right lower chest is very characteristic. The condition is often mistaken for pneumonia consolidation. Cabot reports the frequency of this complication at .3-.4%. The cause is usually Staphylococcus aureus, not B. Coli as might be expected.

5. Pleuritis is the most common thoracic complication. Wolbrecht reports its incidence in 38% of cases.

6. Bladder and Renal complications are fairly common. The most common early manifestations of these are acute retention of urine and painful micturition.

As Willis points out, much is being done to educate the laity concerning cancer when 80% of deaths from malignancy occur after fifty years of age, and yet nothing is said about appendicitis in which 80% of deaths are under forty years. Rowlands points out that education of the public is the only adequate method of coping with the disease. At present the doctor is often not called until the most favorable time for operation is passed or until purgatives have been given.

Sir William Osler crystallized the position of physicians when he wrote, "There is no medicinal treatment for appendicitis"; and again, "every case of appendicitis should be operated on; the date of the operation alone may vary," in the words of Lejars sums up the general attitude of the profession on the treatment of appendicitis. There are two safe times to operate, first within the initial 24-36 hours, and second after the inflammation has sub-

sided. Adams sums up the operative procedures in early cases thus:

1. Acute appendicitis limited to the appendix — appendectomy without drainage.

2. Acute appendicitis with local peritonitis and pus formation—relief of tension with subsequent appendectomy.

3. Acute appendicitis with general peritonitis—appendectomy with cleansing of the peritoneum and perhaps temporary drainage.

In the second group a number of good surgeons advocate appendectomy, cleansing of the peritoneum with no drainage. The question of drainage is often difficult to decide. In all probability it is often carried out where it is not necessary. The discussion is an old one and is still not settled. The earliest suggestion that removal of a gangrenous appendix in the presence of purulent peritonitis could be treated conscientiously without drainage was made by Mikulicz in 1884. However the axiom of Lawson Tait is still looked on with favor, namely, "when in doubt, drain."

In late cases conservative treatment should be employed, as limiting adhesions will usually form and drainage of a localized abscess has a lower mortality than operation for a spreading peritonitis due to appendicitis. Such treatment should include absolute immobilization in Fowler's position, nothing by mouth, no purgatives or enemata except for 5% saline per rectum, hot fomentations for pain. However Lejars recommends continuous application of ice bags to the abdomen. Rowlands claims that in two-thirds of these cases the symptoms subside and operation can be done within a week. In the other third there is no improvement and the surgeon is forced to operate.

In young children and in the aged, such temporizing is considered poor treatment as their resistance is lower. Appendicitis in children is insidious in onset and the tendency is toward rapid perforation. The omentum in children is relatively small and hence localization of the peritonitis is not so apt to occur as in an adult. Thus immediate operation is the treatment of all cases of appendicitis in children and in the aged.

Prognosis depends on early diagnosis and proper treatment. Delay and ice bags in appendicitis plays the same role as delay and salves in cancer. The average mortality given by a group of authorities is 4.23%. If the condition is recognized and operation performed within twenty-four hours the mortality drops to .9%. Adams makes this figure as low as .5%. This, however, is increased to 10% with a delay of two or three days. The prognosis is influenced of course by the pathology present at the time of operation. Burgess gives the following figures from the Royal Infirmary in England:

	Mortality
1. Removal of acutely inflamed appendix without drainage	2.07%
2. Appendicular abscess; appendectomy with drainage	4.7 %
3. Appendicular abscess; drainage only	16.6 %
4. Appendicitis with diffuse peritonitis; appendectomy with drainage....	16.9 %

The greatest mortality occurs between the ages of five to fifteen years. The younger the child the greater the mortality. The rapid course and the tendency to early rupture with diffuse peritonitis partly explains this. The frequent use of cathartics and the difficulty in early diagnosis in children play an important part in raising the mortality.

Conclusions.

1. A clear understanding of the pathology of appendicitis is very essential to the practitioner, bearing in mind especially the lack of correlation between the pathological condition and the clinical picture.

2. Appendicitis occurs at any age

but most commonly from fifteen to thirty, predominating in males in a ratio of 2:1.

3. Appendicitis occurs chiefly in England, Canada and the United States, where a modern high protein diet is taken. It is relatively uncommon in peoples whose diet is simple, consisting chiefly of vegetables with a high cellulose content.

4. The most important cause of appendicitis is digestive trouble, especially constipation.

5. B. Coli is the most common organism isolated in cases of acute appendicitis.

6. Streptococcus pyogenes is the most important etiological agent.

7. Oxyuris vermicularis is a not uncommon cause of appendicitis in children.

8. Contrary to various reports the modern treatment of appendicitis is not inadequate, since in spite of a great increase in incidence the mortality rate per 1000,000 population is only slightly increased.

9. The classical symptoms in order of occurrence are pain, nausea and vomiting, tenderness, rigidity, fever, and leucocytosis; pain being the most constant.

10. Prophylactic treatment is a dietary matter. The most important factor however in reducing mortality is in education of the public as to the value of early diagnosis and operation. Early operation, within 24-36 hours of the onset is the ideal treatment. Cases seen later than this should be treated conservatively until the acute inflammation has subsided, with appendectomy at this stage. This latter is not true however in children or elderly persons who should be operated upon when diagnosed.

11. The mortality of early operative cases is less than 1%. The mortality in children is high, due to the difficulty in early diagnosis, frequent use of cathartics, and the tendency to early rupture and diffuse peritonitis.

The Relation of the Thyroid to Other Ductless Glands.

R. Appel, 2T9.

The Adrenals: The administration of adrenal to the human being produces many of the clinical phenomena coincident with Graves disease. The rate of metabolism is heightened, blood pressure is elevated, tachycardia occurs, sweating is increased, and finally nervous energy is greatly intensified. With these facts in mind Crile suggests that it is thyroxin that sensitizes the tissues to adrenalin. The drug increases hyperthyroidsm; hyperthyroidism increases adrenalism; in other words, adrenalism, iodism, and hyperthyroidism coexist, each condition augmenting the other.

Kendall in seeking to establish relationship between the thyroid and other glands of internal secretion has assumed that the problem is concerned with nitrogen metabolism, which he has proved to be associated with the function of the thyroid gland. He states that the removal of the parathyroids produces a disturbance in the nitrogen metabolism; nitrogen compounds not normally present in the urine appear, and the percent of the various N. constituents is greatly altered. Removal of the pancreas causes an increase in N. metabolism. Removal of the adrenals and hypophysis results in changes in metabolism and death. Kendall concludes:

"The formation of intermediary products between ammonia and urea and probably other N. constituents of

the urine is brought about by the secretion of the endocrine glands. The thyroid hormone is involved in the first split of ammonia from the amino acids. The adrenal cortex secretion then converts this substance into some other product and the secretion of the thymus, the parathyroids and other glands (ductless) are involved in the further elaboration of the N. constituents which finally appear in the urine. It is evident therefore, that the administration of thyroid hormone merely starts an increased rate of production of ammonia, which in itself does not produce hyperthyroid symptoms. It is only when the other ductless glands are stimulated that the reaction is carried on at a rate sufficient to change the basal metabolism, the irritability of the nerves and the other effects produced by the administration of the thyroid hormone."

Herring fed cats with thyroid and obtained an increased output of adrenalin. Connors and Cottel believe that injections of adrenalin increase the secretory power of the thyroid. Crotti believes that there undoubtedly exists an interrelation between the thyroid, pancreas and adrenals. The adrenals are reciprocally stimulating, the thyroid and pancreas inhibit each other, while the pancreas and adrenals are antagonistic.

The Parathyroids: For many years considerable controversy existed regarding the relationship of the parathyroids to the thyroids, but the most recent work tends to show that each has a definite and separate function. That no distinct hypertrophy of the parathyroids follows thyroidectomy was the conclusion reached by Vincent and Arnason in 1920.

In an exhaustive review of the literature Bothby concludes that the only relationship seems to be anatomical and not functional; the parathyroids are not embryonic thyroid tissue. Experimental evidence pointing to the parathyroids as the primary cause of idiopathic tetany is very limited in cases unassociated with operative procedures on the thyroid.

The Thymus Gland: That our knowledge of the thymus gland and its relation to the thyroid is of theoretical and not practical importance is evidenced by a review of the literature. European scientists are more extravagant than the American investigators. Crotti believes that a close relationship exists between hyperplasia of the thymus and thyrotoxicosis and this view has also been supported by many workers. After thymectomy in animals, the thyroid gland tends to become hyperplastic as in Grave's disease, and likewise following thyroidectomy the thymus becomes hyperplastic. This fact Crotti believes is of great importance since it explains why, after an operation for goiter, it may be necessary to deal with the mechanical as well as functional disturbances due to an increased thymic hyperplasia. He states that as a consequence of this he routinely explores the upper mediastinum following thyroidectomy, and removes the thymus whenever it is found. He believes that not only are the remote results of operation better, but that the operative course is also more satisfactory because of the elimination of choking spells of thymic origin.

The idea of the close surgical relationship of thyroid and thymus glands as supported by Crotti, is interesting, but as yet has not received the practical support of the American surgeons. Neither Crile nor Halsted mention thymectomy in their work on the thyroid gland and the subject is conspicuous by its absence in the writings of Bartlett, Haggard, Judd, Mayo, Ochsner, Lahey, Lewis and others.

Pituitary Gland: That a definite interrelationship exists between the thyroid and pituitary glands seems probable. In 1922 Anders & Jameson reviewed the literature and found that an associated disturbance of the thyroid function occurred in 33 per cent. of the cases of acromegaly that were studied. Their investigations indicate that hypo-

thyroidism is more commonly associated with acromegaly than is hyperthyriodism, and that those cases which manifest myxedematous features are decidedly improved as the result of the use of pituitary preparations.

From the results of other investigators, Crotti concludes that the removal of the thyroid hastens growth, causes hyperplasia of the hypophysis retards growth of the thyroid, prevents metamorphosis and retards the development of the cutaneous pigment. Vaso-motor disturbances, variations in temperature and increased sensation of thirst are observed in disease of the pituitary as well as in disease of the thyroid. It is probable that the disturbed metabolism of fat and the cutaneous eruptions in Grave's disease are due to disturbances of the hypophysis.

Tierney and Englebach have noticed that both subjectively and objectively the function of the pituitary gland is dualistic. Thus, disease of the gland may cause amenorrhea, dysmenorrhea, epileptiform attacks, somnolence, obesity, headache, definite changes in the osseous, genital and dermal systems, increased blood pressure, fever, and involuntary muscular contractions. The analogy between these syndromes and those coincident with disturbances of the thyroid is evident. Moreover, in the majority of cases of clinical hypopituitarism there is a decreased Basal Metabolic Rate.

Pancreas: Although there is a great deal of experimental data to indicate a close relationship between the thyroid and pancreas, diabetes and hyperthyroidism are comparatively rarely associated. Fitz found that hyperthyroidism and diabetes in the same person are only associated in a small number of cases, and then only by chance. On the other hand, disturbances in Carbohydrate metabolism are not uncommonly noted in Grave's disease has been attributed to a disturbance in the normal function of the pancreas. Some investigators have reported changes in the hostology of the pancreas in animals after feeding them with gland. Others fail to support this view.

Jackson at the Mayo clinic had several cases of exophthalmic goiter, as well as adenoma with hyperthyroidism, associated with diabetes. In all these cases diabetes was successfully controlled by diet and the administration of insulin preparatory to thyroidectomy. Following operation the prognosis was very favourable with regard to cure for diabetes as well as hyperthyroidism.

Primary Carcinoma of the Lung *

K. A. MacLean.

A review of the literature on the subject shows that we probably have to go back to Morgagni (1682-1772) as the first to publish a report of Primary Cancer of the Lung. Following his lead many French and German writers described cases but these in the light of our present-day beliefs might very well have been cases of Tuberculosis. Laennec, by perfecting the methods of clinical examination, and still later workers on the histological and pathological sides of this condition, eventually brought the disease on a firm footing. Virchow (1853), should be mentioned particularly for the brilliant work on the pathological side that he accomplished. Coming down to more modern times, Alder published a book on this subject in 1911, reviewing 374 cases, which he had found in the literature up to that date. Since then various workers all over the world have

*A paper presented in the Sixth Year, 1927-28.

from time to time reported cases until now, in the report of the above case J. H., we are able to make certain comparisons with the typical case.

Statistical studies at any time are always open to great questioning; and especially might this be true in any attempt by such means to study the prevalence of Primary Cancer of the Lung. This is due not only to the diversity of the observers, but largely to the fact that numerous cases of Lung Carcinoma each year doubtless are diagnosed Tuberculosis, owing to its own frequency and the similarity of the clinical picture.

Likewise, even when autopsies have been done, the gross appearance of the lesions—dense pleuritis adhesions, with necrotic material filling cavities(and fine nodules scattered about—has undoubtedly fooled even the pathologist into thinking the clinical diagnosis correct; and because the ordinary case of Tuberculosis is so uninteresting sections are not even taken—and so is lost the only chance of proving it Carcinoma. There seems no doubt from studying various reports that such conditions occur, and so statistical studies of the incidence of this condition are open to question. However, it would appear that Primary Carcinoma of the Lung is on the increase. Certain authorities state that it owes its statistical increase to: (1) better diagnostic methods, and (2) increased human longivity. They therefore claim it is more apparent than real. It has been the experience of the Department of Pathology at the Toronto General Hospital to encounter malignant disease of the lung (primary), more frequently in recent years than in the past.

The table on the opposite page is a statistical study showing the percentage of Primary Carcinoma of the Lung from a large series of autopsies.

Etiology:

The Etiology of Lung Carcinoma is as elusive as Carcinoma anywhere else in the body. RACE. It seems the civilized races, particularly the white race, are more prone to be affected than the primitive races, viz., the North American Indians. HEREDITY apparently plays very little part. SEX. Nearly all reports place them as about three times as frequent in men as in women. This may be due to domestic life which usually means freedom from vocations and chemical irritants which might injure the respiratory system.

AGE INCIDENCE.

Age.	Carcinoma.	Sarcoma.
Age not stated	18	9
1-10 years	0	6
10-20 years	6	12
20-30 years	10	14
30-40 years	30	19
40-50 years	78	14
50-60 years	113	12
60-70 years	94	3
70-80 years	23	5
80-90 years	2	0
	374	94

Over 75 per cent. occur between 40 and 70 years.

OCCUPATION. Various reports had claimed that occupations resulting in various types of Pneumoconiosis—Cobalt, nickle and iron predisposed Lung Carcinoma, but any evidence put forth is either too vague or too incomplete to be of any real value.. TRAUMATISM. A single traumatism is practically of no account. Certain writers, however, believe that those places near the 2nd, 3rd and 4th bifrications of the bronchi, especially on the right which are subjected to chronic irritations of various sorts are nearly always the site of early bronchial carcinoma. Malignancy of the lung has often been thought to develop secondarily to a chronic bronchitic or tuberculous condition.

Pathology:

In describing the Pathology, one remembers the three types of epithelium found in the lung. (1) The columnar cells lining the bronchi; (2) the glandular lining the mucous glands in the

bronchi; (3) the flattened or cuboidal cells lining the alveoli.

Many authors have offered classifications for pulmonary tumors but they have been of little use. Because of the fact that cell characters vary considerably within the same specimen one is apt to obtain a wrong impression should the tumor mass be not most carefully examined. Probably one of the easiest and most sound classifications is as follows:

1. Columnar Celled Carcinoma.
(a) Simple Carcinoma.
(b) Adeno-carcinoma.
(c) Scirrhus Carcinoma.
(d) Medullary Carcinoma.
(e) Alveolar Carcinoma.
(f) Colloid or Gelatinous Carcinoma.
2. Squamous Cell Carcinoma. (Cancroid).
3. Mixed Type.

The commonest type is the Adeno-carcinoma. This may arise from the bronchial or mucous gland epithelium near the hilum. It extends by radiating out along the lymphatics into the adjacent lung tissue, and soon involves the pleura, resulting often in a plural effusion. Arising as they do from the bronchi, they soon cause stenosis, thereby putting out of commission large lung areas. These collapsed areas are particularly prone to secondary infections. These carcinomata are usually found in the lower lobes, occasionally in the upper. The structure is that of a more or less typical gland-like mass. These glands are lined by one or several layers of cylindrical cell epithelium often cellular and mucous detritus in various stages of degeneration fills in the lumen of these glands.

Then we have the type arising from the pulmonary epithelium of the alveoli, this is spoken of occasionally as the Lobar Type. It arises outside the bronchial tree and may start in an old cavity. It usually increases in size until the whole lobe is involved—this being recognized as the diffuse type. In contra-distinction to this we have the nodular type which results in a scattering throughout the lung of small nodules, varying in size from a small pea to a pigeon's egg. Pleural effusions are not so common in this type and it is usually found in the upper lobes rather than the lower. The structur varies. The diffuse form shows a partial or complete filling of the air vesicles with the cuboidal or squamous cells. The nodular type shows groups of slightly dilated air vesicles filled with papillary projections of the cuboidal cells.

Clinically the significance of the above pathology is well brought out by Lilienthal in an article who states that the bronchial type gives the earlier

Reported by	No. of Autopsies	Date.	% Ca. Lung.
Reinhart (Dresden)	8,716	1878	.057%
Fuchs (Munich)	12,307	1854-1855	.065%
Paessler (Breslau)	9,246	1881-1894	.183%
Wolf (Dresden)	20,116	1852-1894	.223%
Rolleston & Trever (St. George Hospital)	3,983	1890-1902	.050%
Oerstrom (Berlin)	10,272	1900-1907	.31%
Briese (Chemnitz)	12,971	1898-1916	.46%
Univ. of Minnesota	4,362	1919-1921	.300%
Univ. of Minnesota	1,003	1919-1921	.90%
Leipzig	307	1900-1923	5-11%
Leipzig		1924	15%

symptoms because of endobronchial irritation. The cough is dry at first, but soon is accompanied by an increasing amount of glairy sputum. On rare occasions there may be haemoptysis. This train of symptoms changes when the lumen of the tube becomes obstructed and bronchiectatic dilitation develops, with a profuse discharge which quickly becomes putrid. Peribronchial abscesses and supporative pneumonias are further complications pretty sure to arise. By this time the diagnosis will be apt to rest with the bronchiectasis, or lung abscess and the primary cause be overlooked. In contrast to the pronchial neoplasm, the Carcinoma may begin in the alveolar portions of the lung and show no symptoms at first. Later a cough occurs as secondary invasion of the bronchi, by direct extension or by pressure from the mass outside the bronchus, occurs. Bronchiectasis then with its usual repulsive train again develops. Primary tumors of the parenchyma then may develop to a surprising size before showing the characteristic signs and general breakdown in the patient's health that lung carcinoma commonly does.

Metastases:

The following is a table showing the frequency of occurrence and location of metastases in Adler's series of 374 cases of Lung Carcinoma:

(1)	Lymph Nodes	117
(2)	Liver	103
(3)	Lungs	66
(4)	Kidneys	58
(5)	Luprarenals	38
(6)	Brain	28
(7)	Dura Mater	10
(8)	Bones	5

Briese in his series of sixty cases found twenty-one organs affected by metastases. The following are some of these in their order of frequency:

(1)	Regional Lymph Nodes	43
(2)	Liver	25
(3)	Pleura	17
(4)	Kidney	17
(5)	Lungs	11
(6)	Brain	11
(7)	Bones	9
(8)	Ovary	7
(9)	Suprarenals	6
(10)	Dura Mater	3

From the above tables it may be concluded that metastases of Primary Carcinoma of the Lung may be very widespread. That the Lymphatic system is the commonest site for secondaries to appear is the finding of most investigators. One can only suggest that the frequency with which secondaries are found in the liver is in the main due to a spread by lymphatics or direct extension. The frequent occurrence of cerebral metastases from primary pulmonary cancer, as compared with cancers from elsewhere in the body, is likely due to the absence of a barrier between the lungs and the brain, they are as a rule haematogenous in character. Metastases from elsewhere in the body on their way to the central nervous system, pass primarily through the "sieve" of the lungs, in which they are usually immured and not infrequently perish.

Symptomatology:

The common early symptoms are cough, expectoration, pain in the chest, shortness of breath, and later these are associated with constitutional symptoms which characterize malignant disease in any part of the body, that is, loss of strength, loss of weight, loss of appetite and slight fever. The pain in these cases is as a rule due to a pleurisy, but certain investigators have found a unilateral intercostal neuralgia, or a pain in the shoulder or arm not infrequently. Some cases present gastro-intestinal symptoms much like tuberculosis. The dyspnoea, bronchitis and bronchopneumonia occur later. Pressure symptoms, of course, can arise from the mediastinal tumor or from pleural effusion. Hoarseness and the laryngeal type of cough occur in the later stages when the recurrent laryngeal nerve is effected. Nearly all the cases in the Toronto General Hospital showed a

Leukocytosis of 15,000 to 20,000. The differential smear showed on the average about 85% polymorphs present. The sputum is usually a mucoed or mucopurulent type. It is frequently blood-tinged. Frank haemoptysis are uncommon. Tumor cells, often much degenerated however may be found in the sputum occasionally. Bilateral clubbing of the fingers occurs in nearly all cases.

The general course of the disease is a cough persisting from an ordinary cold or influenza or some such respiratory affection, becoming progressively worse, and the condition not infrequently is diagnosed Tuberculosis. It is here held that Tuberculosis rarely if ever predisposes to lung malignancy, a point which is strongly stressed in the etiology of carcinoma of the lung by excellent authorities. The above symptoms progress slowly as a rule, but steadily, causing death of the patient in about one and a half years. The extremes in a series of seven cases from the Toronto General Hospital in recent years, was four months to two and one-half years. The more acute phases of the final illness usually lasted from four to six months.

Physical Findings:

These vary according to the stage at which the patient presents himself or herself for examination. In the early stages, cough and difficulty in breathing directs one's attention to the chest. These symptoms are produced by the extension of a growth in the bronchi. These symptoms are produced by the extension of a growth in the bronchi. This may extend up through a main bronchus to obstruct the trachea, or as is more frequently the case, the secondary involvement of the mediastinal glands compresses the trachea. Some believe there is no fewer in uncomplicated cases, but usually there is sufficient bronchitis, bronchiectasis, etc., to produce a low remittent or intermittent fever. Usually when the patient is examined an area of dullness can be found. Occasionally slight bulging over the affected part is present, but as a rule that part of the chest is flatted-ed and shows diminished movement. On palpation a sense of resistence is found. Vocal fremitus and breath sounds are decreased or absent. The breath sounds are distant and bronchial in character; they are accompanied by very few adventitious sounds. In a certain number of cases a pleural effusion is found. In the areas adjacent to that affected, one gets the signs of lung collapse, bronchopneumonia or bronchiectasis. The chief complications are:

(1) Metastases to other vital organs.
(2) Pneumonia,—acute or chonic.
(3) Gangrene.
(4) Septicaemia.
(5) Hemorrhage.
(6) Localized oedema.

A clinical classification might be given as follows:

(1) Acute Pleuropneumonic Carcinoma ("galloping" form).

This type runs a very rapid course. Beginning with cough, dyspnoea and pain and results in death within four to eight weeks. The lungs and pleura are studded with miliary nodules. Fortunately this type is rare.

(2) Chronic Pleuropneumonic Carcinoma (common form).

(a) Pulmonary form begins as a bronchitis, later dullness and flattening of the chest occurs to be followed by bronchiectatic signs.

(b) Mediastinal form, this may arise in a bronchus but it rapidly presents the picture of a mediastinal tumor.

(c) Pleuritic form, those present signs of a pleural effusion early. On aspiration the fluid is generally clear and yellow in color, but sooner or later it becomes bloody in character. Occasionally tumor may be found in it.

One should probably make especial reference to two of the present day methods of diagnosis that should be used. Diagnosis of Primary Carcinoma of the Lung, to-day is based on

(1) Clinical data, which includes history, symptomatology, course and physical signs, and (2) Laboratory methods such as bacteriologic examination of expectorated material, roentgen-ray examination, bronchoscopy and intratracheal injection of iodized oil.

X-Rays:

These will usually show up any parenchymatous growth before it has even produced a cough. It should be clearly understood too that the unexplained lump occurring in the parenchyma may have the same significance as the lump found in a woman's breast. If on top of this a cough is present then malignancy must be ruled out. Serial plates may be taken and the progress of the lump watched. If it is malignant then the only hope for the patient lies in its early diagnosis when removal by lobectomy or some such procedure is possible.

Bronchoscopy is another method which may prove of great use. The bronchial type of growth is usually placed in such a region that it is hard by X-ray to demonstrate until dilation and often infection of the distal parts of the bronchial tube has occurred. This would then show up as a triangular cone of involved lung just as is found in the case of a foreign body. Before this however it is often possible by the bronchoscope to view the small growth and better still, remove a small portion of it for histiological examination.

Prognosis:

Several of the writers state that ninety-nine per cent. of these cases are fatal, others say cure has never been affected. The census of opinion here is that once malignancy of the lung has been definitely established it is "hopeless." Even by radical surgical or radiation methods very few cases of five years cures are reported.

Menstruation.

A Review of the Anatomy, Physiology and Histology.

H. R. Ziegler.

It is the purpose of this paper to present an outline of the physiology of reproduction with special reference to the Menstrual Cycle in the human female. In order to clearly understand the physiological aspect of the problem I have deemed it advisable to touch on the blood supply and histology of the Ovary and Uterus.

Anatomy:

(a) The arterial supply of the Uterus is derived mainly from the Uterine arteries, branches of the anterior division of the Internal Iliac, together with anastomatic branches from the Ovarian, Vaginal and Inferior Epigastric arteries. The distribution is such that an arterial plexus surrounds the organ which gives off branches which are remarkable for their tortuous course within its wall.

(b) The venous drainage is from the Uterine plexuses lying along the sides and superior angles of the body between the layers of the Broad Ligament. These plexuses communicate with the Ovarian and Vaginal Plexuses and are drained by a pair of Uterine veins opening into the corresponding Hypogastric veins.

(c) The ovaries are supplied by the Ovarian arteries arising from the abdominal Aorta and forming a free anastomasis with the Uterine artery.

(d) The Ovarian veins form the Pampiniform Plexus between the layers of the Broad Ligament. Two veins

issue ,from the plexus on each side which eventually fuse to form the Ovarian vein. On the right side the vein opens into the Inferior Vena Cava at an acute angle and on the left into the left Renal vein at a right angle.

Histology of the Ovary:

For descriptive purposes the ovary may be divided into four sections: (1) the hilum, (2) the medulla and (3) the Cortex; (4) the Graafian Follicle.

(1) The Hilum is a small area adjoining the Mesovarium. Here the tissues of the Broad ligament pass into the ovary and spread out to form the Ovarian stroma. This consists of fibrous connective tissue rich in elastic tissue and a few smooth muscle cells.

(2) The Medulla is a small semilunar area around the Hilum. It consists of stroma alone containing many large blood vessels and hence is often referred to as the Zona Vasculosa.

(3) The Cortex is formed of radiating stroma from the Medulla interspersed with glandular elements. At the surface of the Ovary the stroma forms a dense layer of fibrous tissue, the Tunica Albuginea. Beneath it is a single layer of cuboidal cells, known from its function as the Germinal Epithelium. The Parenchyma or secreting portion of the ovary consists of a glandular elements, the Graafian Follicles.

(4) The structure of the Graafian Follicle can best be appreciated by a histological study of its development. However probably a brief description of its form in the mature phase will suffice. A cavity is present in the Follicle surrounded by the stratum Granulosum and containing Liquor Folliculi. Into this cavity projects the ovum surrounded by a single layer of cells, the Corona Radiata. The ovarian stroma in the immediate vicinity becomes modified to form a sheath for the Follicle. This consists of an outer fibrous layer, the Tunica Fibrosa or Externa and an inner, more cellular and highly vascular layer, the Tunica Vasculosa or Interna. Maturation of the ovum is completed in the ovary and eventually the Follicle ruptures to discharge the ovum surrounded by the Corona Radiata. Fertilization of the ovum takes place as a rule in the Fallopian tube. The cavity formed by the rupture of the Follicle becomes filled with a blood clot and the former Follicle now becomes known as the Corpus Haemorrhagicum.

This represents the earliest stage in the development of the Corpus Luteum. It consists of large yellow lutien cells containing a yellow pigment, together with a supporting connective tissue and blood vessels derived from the Tunica Interna. The origin of the Lutein cells is not clear. Some observers believe them to be derived from the Tunica Interna while others regard them as a proliferation of the Stratum Granulosum. In its mature state the Corpus Luteum has a definite cellular structure having a supporting Connective Tissue. Blood vessels run in close apposition to the cells and the whole arrangement resembles other glands of internal secretion, being especially similar to the cortex of the Adrenal gland.

Degeneration and absorption of the Corpus Luteum occurs in the later months of pregnancy, and in the event of non-fertilization of the ovum during the period of Menstruation. The Corpus Albicans is thus formed which is eventually absorbed leaving only a small area of fibrous tissue.

History of the Menstruating Uterus:

The wall of the uterus consists of three coats, serous, muscular and mucous, of which we are mainly interested in the last.

The Mucosa of the Uterus is in structure and function unlike any other lining membrane in the body and is constantly referred to as the Endometrium. It presents marked variations in structure dependent on the functional condition of the organ.

In the non-pregnant uterus during the child-bearing period, the Endometrium is in an almost continuous state

of change constituting the menstrual cycle and culminating in the phenomena of menstruation. For purposes of description, however, we can divide the cycle into four phases, viz.:

1. The Intermenstrual Phase or Resting stage of about twelve days duration.

2. The Premenstrual Phase or stage of Preparation of about five to six days.

3. The Menstrual Phase or stage of Destruction of from two to four days duration.

4. The Postmenstrual or stage of Reparation of about six days duration.

And finally, 5. Compare the changes in the endometrium at the occurrence of pregnancy with menstrual changes themselves.

1. Resting Stage:

The Mucosa is 2-3 min. thick and consists of a lining epithelium and a stroma containing numerous glands and blood vessels. The stroma resembles embryonic connective tissue having a rather loose appearance It consists of fine, interlacing fibrils and long irregularly branching cells. The glands are simple forked tubules lined by simple cilated columnal cells, extending through the stroma to rest on the muscularis. They run a fairly straight course near the surface but are slightly tortuous in the deeper layers of the stroma. In cross-section the lumina present an even round border. The lining epithelium of the mucosa is of the simple ciliated columnar variety.

It is of interest to note that in the stroma the vessels are devoid of any fibrous or muscular coats. In fact some observers believe them to be merely channels created by the stroma cells. Moreover the terminations of the arterial vessels lie just beneath the surface epithelium and here also lie the end branches of the venous drainage system. These facts are of importance during the premenstrual phase and probably have some effect in producing the congestion of the stroma.

2. Pre-Menstrual Phase:

This phase is marked by changes throughout the whole mucosa so that it finally reaches a thickness of 6-7 mm. The glands increase in length and width and become very tortuous throughout their whole length. Their lining epithelial cells increase in size and numbers and take on secretory characteristics, being of low type and having frayed edges. The deeper part of the glands become distended with mucous so that in cross section their lumina have an irregular dentate margin. The surface epithelium remains intact and the cells unchanged.

The blood vessels become much distended so that serum and lymph pass out into the stroma which becomes soft and oedematous. Rupture of some vessels and diapedis are factors in the appearance of blood which collects in the stroma and especially near the surface epithelium. The stroma cells increase both in size and numbers and some of these come to resemble the characteristic decidual cells of early pregnancy. The glandular and circulatory changes in the deeper parts of the stroma give to it a rather spongy appearance resembling the Stratum Spongiosum of pregnancy while the superficial part is more compact. All these changes increase progressively up to the onset of menstruation. Just previous to the onset of the succeeding flow Novak[4] has described a dense infiltration of the stroma with Lymphocytes and Polymorphonuclear Leucocytes. In his opinion this is a response to the degenerative processes about to occur in the Endometrium since at this time its upper layers stain more poorly. Earlier stages of this phase show only a sporadic cellular infiltration.

3. Menstrual Phase:

Our present knowledge of the microscopic changes in the human Endometrium during this phase comes as a result of the observation of Novak and Te Linde.[4]

In its earliest stage the surface epi-

thelium is denuded in small areas allowing the escape of blood, etc., which has caused the congestion of the stroma. The glands pour out their profuse secretions which have been distending their lumina. The congestion is thus relieved, and within a few hours the thickness of the mucosa is reduced to 2-4 mm. At this time the epithelial glands of the surface layer, the cells of glands and the stroma cells show typical signs of degeneration particularly in the superficial area. The denudation of the surface epithelium with loss of underlying stroma continues and is accompanied by rupture and actual bleeding of the fine blood vessels. By the end of the second day the loss of tissue has become extensive, all the compact layer and most of the spongy layer being gone leaving only a small amount of stroma containing the stumps of the glands. The loss of such a large amount of the mucosa does not usually occur as an extensive shedding in large masses. The cells first show signs of degeneration and the process is one of molecular necrosis.

4. Post-Menstrual Phase:

Regeneration of the surface epithelium is rapid. Contrary to popular belief it commences before the cessation of bleeding and within 24 hours after bleeding ceases it is completely restored. This is accomplished by proliferation of the intact lining epithelial cells of the remaining gland stumps which grow out to cover the stroma in the interglandular areas. Proliferation of the stroma cells and glands continues more slowly and the endometrium is restored to its former resting stage in about six days.

5. Pregnant Uterus:

In the pregnant uterus the changes in the endometrium are very similar to but more extensive than the premenstrual changes. At present these premenstrual changes are regarded as a preparation for the imbedding and development of the fertilized ovum.

Physiology of the Menstrual Cycle:

Histological examination of the uterus and ovaries, together with clinical observations have shown that between puberty and the menopause woman goes through a periodic menstrual cycle which is explained above. Furthermore, that during pregnancy this cycle is in abeyance. The mechanism responsible for this cycle and evidenced by such clear-cut changes in the Endometrium has for many years been a subject for argument and controversy among physiologists and gynaecologists. And rightly so, for without some clear conception of the why and wherefore of menstruation we would be at a loss to satisfactorily treat disturbances of this very important phase of the life of woman.

In ancient times menstruation was regarded as a periodic process of flushing, by means of which the human female ridded herself of impurities. For this reason she was shunned as a vile creature during the period of menstrual flow. This attitude has in modern times undergone a marked change, so that we now regard these periodic changes in the uterus as a preparation for pregnancy and that menstruation is the monthly abortion of an unfertilized ovum and its decidua. In other words, "women menstruate because they do not conceive."

This modern view of the mechanism of the cycle was originally brought forward by Fraenkel.[5] In brief his theory was that the Corpus Luteum was responsible for the nutrition of the uterus from puberty until the menopause and to prepare its mucous membrane for the maintenance of the ovum. If the ovum be fertilized the corpus lutum is responsible for maintaining the raised nutrition of the uterus during gestation. If the ovum be unfertilized it merely produces the premenstrual changes and then undergoes degeneration. Observers since then have elaborated and changed his original theory, and their conclusions have been based on careful histological and clinical correlation of

the ovarian and endometrical cycles. Experimental work along these lines has been considerably hampered by two main factors. Firstly, the difficulty in using results obtained from work done on laboratory animals, to explain the cycle in humans since the menstrual cycles differ in many respects. And secondly, the obvious difficulty of obtaining uteri and ovaries for observation from healthy women free from any pelvic disease.

We have seen that there is a definite correlation between the ovarian and endometrial cycles and the modern conception of menstruation is based largely o nthis observation. Shaw[6] and many others since, have shown that ovulation precedes menstruation and that the ovum is extruded from the ovary at about the fourteenth day of the cycle. The corpus luteum then develops reaching its mature phase five or six days before the onset of the menstrual flow. During this mature phase the Endometrium undergoes its characteristic premenstrual changes which have already been described. In the event of fertilization of the ovum the corpus luteum develops even farther, becoming conspicuous in gross study of the ovary. At the same time the formation of the decidua results, and excision of the corpus luteum at this stage will as a rule result in abortion. The corpus luteum remains intact until near the end of pregnancy when its degeneration results. In rare cases excision of the corpus luteum during early pregnancy does not result in abortion, a fact which I will explain later. In any event most observers are agreed that the Corpus Luteum exerts a profound influence on the endometrium during pregnancy and prevents the phenomena of menstruation during this period.

In the event of non-fertilization of the ovum, death of the latter occurs. We cannot be sure of the time at which the unfertilized ovum dies but Whitehouse[7] believes it to be at about the 27th day of the cycle. Death of the ovum is followed by evidences of commencement of rapid degeneration of the corpus luteum at about the 28th day. The same author believes that death of the cells of the Corona Radiata surrounding the ovum produces what he terms a "negative phase," which is responsible for degeneration of the corpus luteum. Accompanying this degeneration is the destructive or menstrual phase of the endometrium resulting in menstruation. It will thus be clear that menstruation occurs not as a result of corpus luteum but because of its absence.

This influence of the corpus luteum on the endometrial cycle has now been established as due to a Hormone elaborated by the corpus luteum. Certainly its structure resembles that of other glands of internal secretion. Ovaries both in animals and humans, severed of their nervous connections have been transplanted and grafted to abnormal sites and even to other ovariectomized animals. In all a normal menstrual cycle or pregnancy have resulted,[8] which would prove that the ovary affects the uterus by means of its internal secretion. A hormone has been extracted from corpus luteum in animals but the effects of its injection into animals after removal of the corpus luteum are variable. At present we know that the corpus luteum exerts a very important influence in controlling the menstrual cycle, but its exact role cannot yet be assigned.

Recent work on the Ovary as a gland of internal secretion has resulted in the extraction of a hormone from the follicular fluid and originally called Follicular Hormone. However it has since been found that the same hormone can be obtained from other parts of the Ovary. It has been extracted from Corpus Luteum, during the early development of this body but is not present during its final mature phase. Of late this substance has been referred to as an Ovarian Hormone and has been isolated from other tissues of the body as well by Allen and Doisy.[9]

In recent years work on the men-

strual cycles of laboratory animals has been markedly stimulated by the work of Stockard and Papanicalaou,[10] and later Long and Evans.[1] They perfected a very simple method of taking vaginal smears by means of which the actual period of the menstrual cycle of laboratory animals could be calculated. As a result of experiments along these lines it has been found that normal men strual cycles in ovariectomized animals can be maintained by injections of Ovarian hormone. However, the presence of corpus luteum is necessary for pregnancy. The subject has been carefully investigated by Allen and Doisy,[9] and their results corroborated by many others. There seems little doubt at present that the menstrual cycle in lower animals is dominated by the Follicle alone while the corpus luteum becomes important only after impregnation. But, in the human on the other hand the presence of a corpus luteum would seem to be of more importance in the control of the menstrual cycle.

Observations made chiefly by Corner[12] and Allen,[00] working with a species of monkeys, Macacus Rhesus, having a menstrual cycle almost identical with humans are especially interesting. Corner found that two types of menstruation occurred. One in which the characteristic premenstrual changes of the endometrium were absent, with no evidence of a preceding ovulation or the presence of a Corpus Luteum. The other type showed the usual premenstrual changes, together with evidence of a preceding ovulation and formation of the Corpus Luteum. In the first instance it is believed that the bleeding occurred solely under the influence of the Ovarian Hormone since it was not preceded by the formation of a Corpus Luteum. Thus it would appear that there are two types of cycle in this species of monkey—one dominated by the Follicles and not dependent on ovulation and the other controlled by the Corpus Luteum. Moreover it would seem that even the same animals may at different ages and under different environmental conditions exhibit different types of cycle. It would also appear that in rare instances this primitive form of Follicular cycle persists in humans in whom no evidence of ovulation or the formation of a corpus luteum preceding menstruation exists.

In any event Novak[14] has recently advanced the theory that the menstrual cycle in humans is controlled both by Follicular Hormone and the hormone of Corpus Luteum. That there are two such distinct hormones is an acknowledged fact. He claims that the Follicular Hormone is responsible for the early premenstrual changes of the endometrium and these reach their climax under the influence of the hormone of corpus luteum. As a support of this theory he has in two striking cases of Amenorrhoea due to ovarian hypofunction established a normal menstrual cycle. The treatment comprised twelve daily injections of Follicular Extract, followed by six daily injections of Corpus Luteum Extract and one more of Follicular Extract. This series of injections was followed on the next day by a normal menstruation. One week after the flow ceased the same treatment was resumed with a similar result. Later, discontinuance of this treatment resulted in amenorrhoea. The treatment was then resumed again. In both cases injection of either extract alone did not result in menstruation.

In conclusion it must be admitted that authorities have not yet completely solved the physiology of menstruation. A review of the literature shows that all agree that the menstrual cycle is controlled by an internal secretion of the ovaries. The exact nature of this control still remains as one of the mysteries of Science.

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EDITORIAL.

PROFESSOR J. J. R. MACLEOD.

Professor J. J. R. MacLeod who for a number of years was in charge of the Department of Physiology at the University of Toronto has now assumed a similar position at the University of Aberdeen—his Alma Mater. During his stay here Professor MacLeod did much for the advancement of Physiology both by his personal work and through the work of those associated with him. His success was by no means limited to this for he won the respect and admiration of the students through his geniality, and untiring efforts in their interests.

The inspiration of his presence and activity is gone, but the memory of him, and the stimulus he afforded us to greater heights, will always be with us. We wish good luck and fortune, and hope that across the thousands of miles that separate us we may not be forgotten.

CLASS OF 1934.

To the class of 1934 the Journal extends greetings and best wishes for a safe journey through the Temple of the Aesculapians. Times have changed —the medical man of old is indeed no more, but in the heart and mind of the present day medical man the same deep appreciation for the sanctity of his patients' confidences exists.

Advice is rarely appreciated, but that we may not miss the opportunity may we suggest one thing. That work comes first and play afterwards, but we must not forget that play means

health, and that without health you will be of little value to anyone. One can be too serious or too frivolous—the happy medium is a point midway between. Exercise of some sort is an absolute necessity.

Again we bid you pleasant journey.

JOURNAL ARTICLES.

The University of Toronto Medical Journal is so far as we know the only medical student journal in the British Empire with the exception of one published in Adelaide, Australia, consequently it should be a source of constant pride to the undergraduates of our Medical School.

Being a medium of student expression it theoretically should consist entirely of student articles. Manifestly this is impossible, but it is our intention to publish a majority of the articles from the students themselves. Obviously these can not be expected to be entirely original, but rather will largely be a brief review of the more salient points on subjects of particular value to the students. That the writing of such articles will furnish invaluable training none will deny. In later years of active practice one may readily develop, and present articles built on the background of literary knowledge the Journal has given the student authors. An article looks entirely different in print to the figment in one's mind. We hope to be able to advise and assist the students in this expression that we may all in turn benefit thereby.

Without the aid of the members of the faculty our Journal would indeed be a paltry thing. We hope they may assist us in presenting a well balanced Journal. Of particular value to the students are articles summarizing as it were complete topics. These offer to the students in permanent form the matured expressions of faculty opinion, and are, as all we students know, of great aid in the proper understanding of a subject. We hope that any articles Faculty members may have, or care to write will be sent us at the earliest possible date.

CRITICISM.

May we have your criticism this year? We are trying hard to make the Journal entirely satisfactory to all years, and constructive opinions would be of great aid to us.

THE JOURNAL STAFF.

The Journal staff has undergone a mild reconstruction this year. We have introduced a new position on the Editorial staff in the person of an Assistant Editor. It is understood that he will succeed to the Editorial position the next year, and it is hoped that this will give him one year's active training on the Journal instead of merely handing him the position entirely unprepared. We have also given to the Woman's Editor a permanent department on medical history. She has complete authority to manage her department as she sees fit, and it is the intention to present articles written by the medettes therein. The subjects will always be interesting and well handled, we are sure. We are giving medical sports a permanent department, and will try hard to present an interesting review of the medical faculty sports each month. The finances of the journal have been gone into carefully by the Business Manager, and a well planned budget system will be followed throughout the year.

MR. DUNHILL OF ST. BARTHOLOMEW'S.

On October 3, the sixth year had the pleasure of a lecture by Mr. Dunhill of St. Bartholomew's Hospital, London, England.

Professor of Surgery, Clarence L. Starr, introduced Mr. Dunhill as a member of the staff he himself had once been so pleasantly associated with.

Mr. Dunhill's topic was built around the presentation of some original work he is doing on malignancy of the thyroid. Macro-, and microscopic photographs were shown illustrating his subject.

The conclusions drawn were:

1. That malignancy of the thyroid may be extremely slow and one must not be too optimistic.

2. That apparently poor surgical risks may actually not be.

3. That malignant thyroid remnants left at thyroidectomy may be either held in check, or obliviated by X-ray therapy.

4. That we must more carefully treat the so called papilliferous cystadenoma of the thyroid as it really is, carcinomatous.

The Immortal Harvey.

Miriam Brick, Woman's Editor.

At the beginning of the seventeenth century the great University of Padua, rendered famous by associations with Vesalius, Fallaires and Fabricus, was at the height of its renown as a medical centre. It was natural therefore that William Harvey, recent graduate of Cambridge, should choose in 1598 to study anatomy under the great master Fabricus at the most distinguished school in Europe.

Harvey was born at Folkestone, on the south coast of England, in April, 1578, just four years after Fabricus published his treatise on the valves in the veins. Taking his Arts degree from Caius College, Cambridge, in 1597, he left England the following year to study medicine at Padua. An intimate friend, John Aubrey, describes Harvey at this time as "a small choleric man with round face and florid complexion and raven hair — a man full of spirit and withal contemplative." In this university, governed by students of different nationalities, Harvey was elected councilarious for the English nation, a position of which John Finch in 1652 said entailed being drunk at least forty times a year.

In his sympathetic and enthusiastic teacher-investigator Harvey found a life model and firm friend. Fabricus, like his predecessors, viewed physiology through galenic lens, and was thus blind to the obvious and turned a deaf ear to voices crying out recent discoveries, and although he described the valves in the veins accurately, it remained for his pupil, stimulated most by his discovery to weld together the accumulated anatomical links, in order to evolve the great truth of the circulation of the blood.

From Galen until 1615 the physiological landscape was shrouded in a cloud of Galenism. It is true that such names as Vesalius Columbus, Caesalsinus and Fabricus are prominent in the history of that period for individual contributions to the mysteries of physiology, and each in turn refers constantly in his teaching not to his immediate precursor but to Galen, accepting the traditional errors passed in from a far earlier day. Thus we find, at the end of the sixteenth century, anatomists upholding, though a little unconvincingly, the theories that the circulation contained air; the interventricular septum was perforated and that the veins carried blood and vital spirits from the heart to the periphery.

At the beginning of the sixteenth century Harvey obtained his doctors degree from Padua, and returned to London, where in 1802 he took his M.D. at Cambridge, and two years later became a member of the Royal College of Physicians. Both among his fellows, and at court Harvey was received

favorably and was appointed physician extraordinary to James I. An interesting anecdote relates how he accompanied Charles I on his unhappy wanderings and of how during the battle of Edgehill, when in attendance on the prince, Harvey sat on the outskirts of the fight, under cover of a hedge, reading a book.

In 1615 Harvey was appointed Linnean lecturer. These lectures were completed in a six-year period, the course entailing both dissection of the human body and a series of anatomical discourses. Witnessed both by laity and the profession the so-called "anatomies" performed on executed criminals by permission of the crown were more or less a public function. The incomparable Pepys provides an amusing accounte of such a public dissection describing not only the cadaver but the spectators and the large dinner of which everyone partook at noon.

During the Linnean course of lectures Harvey first ventured in 1615 to expound his view concerning the circulation of the blood. It is interesting to speculate why this doctrine remained unpublished for twelve years, then to appear as "Exercitio Anatomica de Motu Cordis et Sanguinis," printed in Frankfurt, Germany, by Wilhelm Fitzer, hitherto unknown as a publisher of medical works. Evidently Harvey anticipated an unfavorable reception to a theory so obviously dealing a death blow to Galenic ideas for "in putting it forward he feared not only injury to himself from the envy of a few out trembled lest he might have mankind at large for his enemies." Aubrey tells us that "when the book was published he fell mightily in his practice and it was believed by the vulgar that he was crack-brained and all physicians were against him."

Harvey was the first to provide a clear and lucid description of the circulatory mechanism. He arrived at this view, led step by step through observations based on his examination of the living animal, or as he tells us by "repeated vivisections." So great were the difficulties encountered in reaching his conclusions that it is said he inclined to agree with Fracastorius, the physician-poet "that the movements of the heart and the like purpose could be comprehended by God alone." However his despair was but momentary, and neglecting the question of spirits previously so closely bound up with the problem of the blood flow, he set himself to find a mechanical solution to a physical phenomenon guided by distinctly quantitative arguments. The great step which was to clarify the whole situation came when he satisfied himself that the quantity of blood driven out from the heart could be supplied in no other way than by a return of the blood from the arteries through the veins.

Once Harvey grasped that the same blood coursed again and again through the body from arteries to veins in the tissues, he found fact after fact to support his view. Now it was clear why the heart emptied when the vena cava was tied; why almost all the blood could be drained away when a single vein was cut, and for the first time the purpose of the valves in the veins was recognizable.

Harvey's work is a distinguished offering on the altar of Truth. Not as a philosopher, but as a scientist, he confined himself to the dissection of nature's fabric. He thus dealt a death blow to the theories and speculations of his predecessors, and stands out for all time as a brilliant example to future investigators.

The Editor,
University of Toronto Medical Journal,
University of Toronto,
Toronto, Ont.

Dear Sir,—

I wish to call the attention of the members of the graduating year to the fact that the Department of Hospital Service of the Canadian Medical Association has prepared a list of thoroughly modern Canadian hospitals which are offering excellent interneships to recent graduates in medicine.

There are many hospitals, unfamiliar to the students because located away from teaching centres, which offer a service quite equal to that found in hospitals in other countries. Moreover, many Canadian hospitals provide honoria which are very generous. If any of the students desiring a position for next spring would apply to the Canadian Medical Association at 184 College Street, Toronto, either personally or by letter, we would be very pleased to offer them every assistance in obtaining an appointment.

Yours sincerely,

HARVEY AGNEW, M.B.,
Secretary, Department of Hospital Service.

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